An investigation of cognitive impairments in Relapsing Remitting Multiple Sclerosis using an ecologically valid test of executive functioning

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Volume I

Main Research Project And Service Evaluation Project

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Thesis submitted in partial fulfilment of the degree of Doctorate in Clinical Psychology

Institute of Psychiatry,
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July 2013

Acknowledgements

I would like to thank the supervisors of my main research project, Prof Robin Morris and Dr Elaine German, without whom this study would not have been possible. I greatly appreciate their contributions to the research, and the feedback and support they have provided throughout the process of conducting the research. I would like to thank Dr Eli Silber and Ms Kitty McCarthy, who were instrumental in supporting recruitment for the study. Thanks are also due to Dr Daniel Stahl, who provided statistical advice. Most importantly, I would like to thank the people with multiple sclerosis who showed an interest in the study and agreed to give up their time in order to contribute to research despite the difficulties associated with their condition.

I would like to thank Dr Daniel Michelson, who supervised my service evaluation project and provided helpful feedback and support from the early stages. Thanks also go to members of the Child Anxiety Clinic, who gave up their time to participate at various stages. With regard to my clinical placements and case studies, I would like to thank Prof Derek Bolton, Dr Tarick Ali and in particular Dr Grace Wong, who kindly supervised two of my case studies. I also appreciate the understanding and support of Prof Morris and Dr Lucy Maddox, who provided excellent elective placements during my final year of training. I am also grateful for the support provided by members of the course team, including Dr Patrick Smith, Ms Sue Rutter, Carole Barnham, Mark Balham and Dr Idit Albert.

Finally, my heartfelt thanks go out to my coursemates, my partner and my friends; who have provided so much support during a busy and at times stressful period of my life, as well as to my parents, who have supported me in many ways throughout my life and career.

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Main Research Project

An investigation of cognitive impairments in Relapsing Remitting Multiple Sclerosis using an ecologically valid test of executive functioning

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Abstract

Background

Multiple Sclerosis (MS) is a multi-faceted condition which is characterised primarily by demyelination of white matter in the central nervous system. MS is associated with physical, cognitive and emotional impairments, which can have a significant impact on daily functioning. Cognitive impairments are observed in multiple domains, including processing speed, verbal memory and executive functioning. However, previous studies have reported mixed findings in relation to the ability of neuropsychological tasks to detect difficulties in everyday functioning, particularly in terms of executive functioning.

Aims

This study aimed to investigate cognitive abilities in relapsing remitting MS (RRMS) using a novel modification of the Hotel Task, designed to be a more ecologically valid test of executive functioning. In particular, performance of participants with RRMS was compared on high and low executive demand conditions of this task, and was also compared to performance on traditional neuropsychological assessments.

Method

Nineteen participants with RRMS and 19 matched healthy controls completed the Standard and Structured conditions of the Hotel Task, alongside a battery of traditional neuropsychological tasks and questionnaires measuring non-cognitive symptoms and everyday cognitive functioning.

Results

Participants with RRMS performed similarly to healthy controls on the executive functioning variables of the Hotel Task, although with a significant deficit on the prospective memory task. Participants with RRMS displayed significantly less efficient performance on both conditions of the Hotel Task compared to controls, and performance did not differ significantly between conditions.

Conclusions

These results were interpreted as evidence that RRMS is not associated with a disproportionate impairment in planning and multitasking, although specific impairments in prospective memory may be present. The Hotel Task holds some promise as a sensitive measure of cognitive difficulties in people with RRMS. Implications and suggestions for future research are discussed.

1 Introduction

1.1 Overview of Chapter

This section aims to provide relevant background information about Multiple Sclerosis (MS) before reviewing the literature on cognitive impairments in MS and introducing concepts relevant for the assessment of executive functioning.

MS will be introduced initially, with particular emphasis on explanations for the breath and heterogeneity of associated symptoms. A brief clinical description of MS is provided, followed by information on the prevalence and incidence of MS in the UK and a short summary of the current understanding of the causes of MS. Next, a summary of the wide ranging functional impact of MS is provided, covering the physical, emotional and social consequences of the condition. Employment and MS will be discussed, before moving onto summaries of the most commonly observed cognitive impairments. The empirical findings on the status of memory, speed of information processing, attention and working memory will summarised, before providing a more detailed summary of the emerging findings from research on executive functioning in MS. Inconsistencies in the findings are noted, and one possible reason for this is presented: limitations in how executive functions are assessed. The section ends by detailing information on complimentary types of assessment, before presenting the aims of the current study.

1.2 Multiple Sclerosis

1.2.1 Description and Clinical Features

MS is considered primarily an inflammatory disease of the central nervous system (CNS), which is characterised by widespread lesions or plaques in the

brain and spinal cord. MS primarily affects white matter but has also been shown to involve grey matter damage (Pirko et al., 2007; Zivadinov & Pirko, 2012). White matter refers to the component of the CNS mostly made up of myelinated axons. Myelin is an insulating tissue which surrounds axons in a 'sheath' which serves to increase the speed at which electrical impulses move from neuron to neuron, and thus has a role in communicating between different areas of the brain (Fields, 2008). Demyelination refers to the damage of myelin sheaths in the CNS, leading to poorer conduction of signals. Grey matter refers to the component of the CNS consisting mostly of neuronal cell bodies and is involved more directly in specific brain functions (Purves et al., 2011). Damage to grey matter typically involves neuron damage and cell loss.

Demyelination of white matter and, to a lesser degree, lesions in grey matter cause the impairments seen in MS and lead to a broad range of effects. As the damage can occur anywhere in the brain or spinal cord, a wide range of symptoms can be associated with MS. Some of the most commonly reported neurological symptoms include numbness, bladder dysfunction, sexual dysfunction, vision problems, pain, as well as gait, coordination and balance problems (Compston & Coles, 2008; Noseworthy et al., 2000). Fatigue is also commonly reported (Bakshi, 2003; MFIS, 2012), along with cognitive (Guimarães & Sá, 2012) and psychiatric changes (Jefferies, 2006; Haussleiter, Brüne & Juckel, 2009). There is great individual variation in the profile of CNS lesions and symptoms experienced by people with MS (e.g. Lucchinetti et al., 2000), as well as the clinical course the condition takes.

As many of the signs and symptoms of MS are non-specific, it is important to carry out differential diagnostic checks. At present, clinical evidence is considered sufficient for diagnosis, although other assessments (such as magnetic resonance imaging [MRI] scans) can help to clarify the diagnosis. In the past, evidence of at least two 'attacks' was necessary for a diagnosis of MS, but currently it is possible to demonstrate the occurrence of one attack and the development of new plaques over time on MRI scans (Compston &

Coles, 2008). If there is evidence of only one acute episode suggestive of demyelination, patients are considered to have a 'clinically isolated syndrome' (CIS). Between 30 and 70% of those presenting with a CIS later receive a diagnosis of MS (Miller et al., 2005).

There is no known cure for MS, and thus interventions involve symptom prevention and management. Prognosis in MS is difficult to predict and varies between individuals with the condition. The life expectancy of those with MS is on average 7 to 14 years lower than the typical population (Goodin et al., 2012), and the cause of death is attributable to MS in more than half of cases (Brønnum-Hansen, Koch-Henriksen & Stenager, 2004). Research also suggests that there are gender differences in the clinical features and prognosis of MS, with males displaying later onset of symptoms and a more rapidly progressing disease course (Greer & McCombe, 2011). Multiple Sclerosis is associated with a large economic burden, in addition to reduced quality of life for people with the condition (e.g. Karampampa et al., 2012).

There have been many terms used to define the clinical course of MS; however one of the most commonly used set of categories divides MS into four subtypes (Lublin & Reingold, 1996). Research noting differences between these subtypes suggests they are important for conducting research and making treatment decisions.

Firstly, Relapsing Remitting MS (RRMS) involves unpredictable and acute exacerbation of symptoms, commonly referred to as relapses. RRMS is the most commonly diagnosed form of MS at onset, with 85% of patients receiving this diagnosis initially (Lublin & Reingold, 1996). The deficits experienced during a relapse typically resolve during periods of relative remission, where remyelination can occur, but there may be persistent deficits in some cases, particularly with regard to cognitive dysfunction (Patti, 2009). The risk of lasting effects appears to increase over time. The length of remission periods typically last for months or years, although factors such as

pregnancy and viral infections may affect the probably of experiencing a relapse (e.g. Buljevac et al., 2002).

Secondly, Secondary Progressive MS (SPMS) describes the continuous worsening of symptoms over time, without the periods of recovery seen in RRMS, and this is associated with gradual worsening of disability (Rovaris et al., 2006). By definition, SPMS develops from an initial period of RRMS. The probability that RRMS will transition to SPMS increases over time since diagnosis, and the median time from RRMS onset to transition to SPMS is approximately 19 years (Confavreux & Vukusic, 2006). It is estimated that 65% of patients with RRMS will develop SPMS (Compston & Coles, 2008).

Thirdly, Primary Progressive MS (PPMS) describes the disease course when there is no remission following initial onset of symptoms (Miller & Leary, 2007). The age of onset of PPMS is later than the onset of RRMS, typically occurring after the age of 40 years (Confavreux & Vukusic, 2006), and this disease course is associated with more diffuse lesions (Nijeholt et al., 1998). Finally, Progressive Relapsing MS (PRMS) is the least common clinical subtype, and involves steady decline in functioning alongside clear acute relapses (Lublin & Reingold, 1996).

1.2.2 Epidemiology

MS is considered the most common non-traumatic disabling neurological condition affecting younger adults (Alonso & Hernán, 2008), typically starting between the ages of 20 and 40. The prevalence of MS is well documented to vary geographically across the globe with a general increase in prevalence with increasing distance from the equator (Rosati, 2001). This variability has more recently be explained in terms of racial susceptibility, with Northern European populations being most vulnerable, although it remains likely that environment has some role in prevalence of the condition also (Pugliatti, Sotgiu & Rosati, 2002). This ethnic variability has been noted over small

geographical distances, for example MS has been found to be more prevalent in Scotland compared to the rest of the UK. In England and Wales, prevalence rates have varied from 74 to 112 per 100,000 at the end of the 20th century (Rosati, 2001). In urban and ethnically mixed population centers, such as London, there would likely be greater variation in the prevalence of MS depending on the demographics of the local population. The Multiple Sclerosis society estimates that approximately 100,000 people living in the UK currently have the condition. The annual global incidence of MS is approximately 3.6 per 100,000 for women and 2.0 per 100,000 for men (Alonso & Hernán, 2008), although this is likely to be higher in Northern European populations. Incidence in the UK has been reported to be 7.2 per 100,000 for women and 3.1 per 100,000 for men (Alonso et al., 2007), indicating a relatively high incidence of MS in the UK.

In terms of gender, a higher number of women have a diagnosis of MS compared to men, and studies suggest that the prevalence of MS is increasing over time for women but not men (Alonso & Hernán, 2008; Sadovnick, 2009). Recently, gender ratios of approximately 3:1 (female to male) have been reported in the literature (e.g. Orton et al., 2006) and this pattern of female predominance is similar to other auto-immune disorders such as rheumatoid arthritis. Interestingly, this gender difference in prevalence varies by age, in that it is less noticeable above the age of 50 years (e.g. Alonso et al., 2007), and by clinical subtype, in that a much smaller gender difference is reported for PPMS (e.g. Miller & Leary, 2007).

1.2.3 Aetiology and Pathogenesis

The cause of MS is not fully understood, but the current view is that MS is triggered by environmental factors in people who have complex genetic-risk profiles (Compston & Coles, 2008). Many environmental factors have been researched, and while no single trigger has consistently been identified for MS, several causal pathways have considered and researched. For example,

there is some evidence that those who have not had certain infections in childhood, such as Epstein-Barr virus, may be predisposed to developing a maladaptive auto-immune response if these viral infections are contracted later in life (Asherio & Munger, 2007a; Compston & Coles, 2008). Other proposed environmental triggers include physical and emotional stressors, climate, vitamin D and smoking (e.g. Asherio & Munger, 2007b; Marrie, 2004).

Not everyone exposed to these environmental triggers develops MS, and this is understood in terms of individual differences in genetic vulnerability to the inflammatory auto-immune response observed in MS. In support of this, there is evidence that family members of people with MS have a greater risk of developing the disease than the general population, with mono-zygotic twins displaying approximately 25 to 30% concordance in rates of the disease (Mumford et al., 1994; Sadovnick et al., 1993; Willer et al., 2003). Nonetheless, most mono-zygotic twins are discordant with regard to MS, and this suggests that while genetics play a role, genetic factors alone cannot account for development of the disease.

Regardless of the cause of MS, the mechanisms underlying the neuro-physiological and functional changes have been widely researched. MS is associated with the formation of a sclerotic plaque, which develops out of a process of inflammation, demyelination and remyelination and other processes such as astrogliosis, an abnormal increase in astrocytes in response to all forms of CNS injury (Compston & Coles, 2008). It is hypothesised that in RRMS, the pattern of relapse and remission is associated with acute attacks causing demyelination, followed by periods of remission where remyelination occurs. However, this remyelination is neither durable nor continuous, and over time impairments can become persistent, with less evidence of full recovery. As the condition transitions to SPMS, more extensive and chronic neurodegenerative processes are observed in addition to demyelination, and this is associated with progressive functional impairments (Compston & Coles, 2008). Nonetheless, there is some evidence

that the mechanisms underlying MS are complex and heterogenous, and that no single pathology explains all cases.

Treatment therefore aims to improve and manage symptoms, and to slow the progression of pathology and disability. At present, the main treatments for RRMS are beta interferones and copaxone, which have been shown to reduce the frequency of relapses and may also slow the progression from CIS to MS and reduce the build up of disability over time (e.g. Kappos et al., 2007). These approaches do not seem to show the same benefit once progression to SPMS has occurred. Clinical trials of medications for MS are continuing.

1.3 Disability and Multiple Sclerosis

1.3.1 Functional Impact and Quality of Life

In the past, the physical disability associated with MS has received most attention when considering the functional impact of this disorder (Butler et al., 2009). For instance, the Expanded Disability Status Scale (EDSS; Kurtzke, 1983), a clinician rated measure focusing mostly on physical disability, is one of the most commonly used measures of functional impact. This physical focus has been criticised, with research suggesting that there has been a mismatch between the priorities of clinicians and patients (e.g. Rothwell et al., 2007), in that patients reported most concern about occupational, cognitive and emotional problems. In the past two decades, a greater emphasis has been placed on the impact of MS on wellbeing and quality of life more generally (e.g. Baumstarck et al., 2013).

When considering general wellbeing, one finding of note has been that people with MS tend to report lower health related quality of life (HRQoL) than people who have other chronic health conditions, such as inflammatory bowel disease, rheumatoid arthritis, diabetes and epilepsy (Hermann et al., 1996;

Rudick, Miller & Clough, 1992). It is again important to note the heterogeneity associated with MS: while approximately 25% of patients with MS never report any impact on their activities of daily living (ADL), up to 15% of patients become severely impaired within a short time of diagnosis (Compston & Coles, 2002). From a health economics point of view, the cost of MS in the UK has been found to be high, and there are significant correlations between QoL, disability and costs of the condition. The respondents in one recent survey reported a mean cost of care over the previous six months of £8,397, mostly due to indirect care, with the cost of lost employment amounting to £4,240 (McCrone et al., 2008).

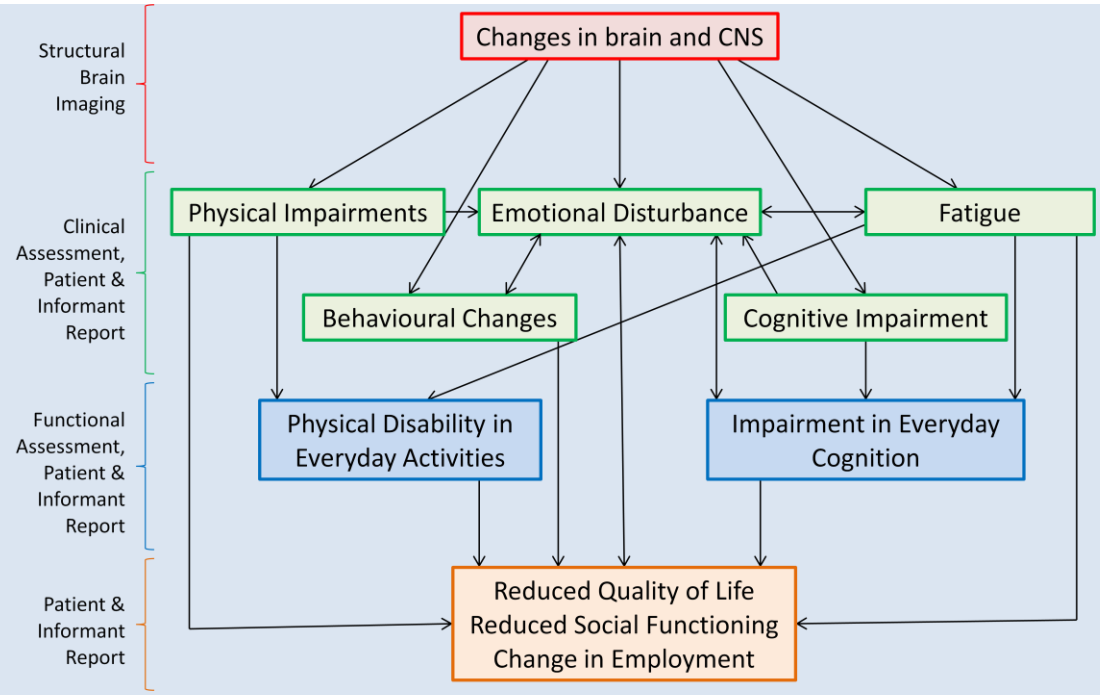


Figure 1: Hypothetical conceptual framework of the impairments associated with multiple sclerosis and the functional difficulties arising from these impairments

The consensus from research to date is that there is no simple predictor of quality of life in MS, and in particular, this cannot be explained purely in terms of physical disability. Rather, it appears that quality of life is mediated by a number of factors, including the impact of the physical, cognitive, emotional and social factors associated with a diagnosis of MS (Benito-León, et al.,

2003), and these factors can interact with each other (Figure 1). These functional domains will be briefly considered below.

1.3.2 Physical Impact of MS

For many people, MS has a significant effect on physical health and functioning, and the physical effects of MS are diverse in nature, affecting functioning in areas such as motor, sensory, sphincter control, sexual functioning and mobility. Research to date suggests that neurological impairment and physical disability account for a modest amount of the variance in HRQoL, and this is independent of the effects of variables such as fatigue, cognitive impairment and emotional changes (e.g. The Canadian Burden of Illness Study, 1998). In particular, sexual and bladder dysfunction have been associated with lower HRQoL in people with MS, even when other forms of physical disability were less pronounced (Nortvedt et al., 2001).

Paltamaa and colleagues (2006) conducted a population based survey of physical functioning in MS and respondents represented 87% of all people with MS in central Finland. This study reported that 82% of respondents reported full independence in self care activities of daily living (ADLs, considered necessary for fundamental functioning). In contrast, 47% of the sample reported some difficulties with instrumental activities of daily living (IADLS; not considered necessary for basic functioning) and 38% of the sample reported that they needed to use a walking aid at all times. There was a large variation within functioning, for example 50% reported being able to walk without any perceived problems while 7% reported being confined to bed due to mobility difficulties. The physical symptom rated as having the greatest impact on daily life was fatigue (36%), with others reporting balance problems (29%) and walking difficulties (28%) as their primary symptom. Sixteen per cent of the sample reported no MS symptoms.

Across studies, one of the most consistent findings has been high levels of fatigue amongst people with MS. This typically refers to a subjective lack of physical or mental energy which interferes with usual or valued activities (Multiple Sclerosis Council for Clinical Practice Guidelines, cited in Kos et al., 2008). A recent global online survey by the Multiple Sclerosis International Federation (MFIS, 2012) found that 86% of participants reported that fatigue was one of their three main symptoms, and that 88% of participants rated the impact of fatigue on their life as medium (43%) or high (45%). No definite pathogenesis of fatigue in MS has been identified, but one conceptual framework is that some aspects of fatigue may arise directly from the brain changes associated with MS (primary fatigue) while other aspects may be best explained as being secondary to poor sleep, changes in psychological functioning or side effects of pharmacotherapy (Kos et al., 2008).

1.3.3 Emotional Impact of MS

A diagnosis of MS holds a lot of uncertainty. Due to heterogeneity in the magnitude and type of difficulties experienced, as well as the unpredictable timescale of relapses and the uncertainties about prognosis, it has been suggested that MS is often experienced as an exceptionally stressful condition (Benito-Leon et al 2003). The uncertainties surrounding MS may lead to patients perceiving a low sense of control over the disease and symptoms. In addition to this, MS is a chronic condition, which is typically diagnosed in young adults and therefore often has great potential to interfere with many aspects of life, including relationships and employment. In keeping with this, the rates of depression and anxiety disorders in people with MS are elevated (Wood et al., 2013).

With regard to depression, there have been consistent reports of elevated depressive symptoms in people with MS. Chwastiak and colleagues (2002) conducted a population based survey of people with MS in the US using the Centres for Epidemiological Studies Depression Scale (CES-D) and found

that 41.8% of the respondents scored above the threshold for depression in the general population, with 29.1% reporting scores predictive of major depression in primary care settings. Other surveys report lower prevalence rates (e.g. 16% of a UK sample; Hakim et al., 2000), although overall depression is about three times more likely in MS than the general population (Jeffries, 2006). Several authors have estimated a life time risk of depression in MS of approximately 50% (e.g. Sadovnick et al., 1996). Research has also suggested that people with MS are more likely to have suicidal ideation and commit suicide than the general population (Feinstein, 2002; Fredrikson et al., 2003). In addition to psychosocial factors associated with having a chronic health condition, there is some suggestion that organic factors may also play a role as rates of depression appear to be higher in MS than in other medical or neurological conditions (e.g. Hausleiter et al., 2009). For example, demyelination has been linked to psychiatric disorders such as depression (Fields, 2008).

Additionally, research suggests that MS is associated with elevated prevalence rates of other affective disorders, such as bipolar disorder, euphora, psychosis and pathological laughter and crying disorder (Hausleiter et al., 2009).

1.3.4 Social and Occupational Impact of MS

Social functioning typically refers to the degree to which an individual is able to interact in their usual way in society and their ability to fulfil their chosen family and social roles (e.g. Hakim et al., 2000). This includes participation in their community and the workforce. There are several ways in which MS can affect social functioning. Disability directly caused by MS can reduce functional skills and mobility, making it difficult to continue in previous social and work roles. Changes in mood associated with MS can also impact on functioning and perceived ability to cope in current roles. If someone with MS leaves employment, this can have a further impact on mood and on finances,

which may negatively affect social functioning. There has been increasing focus on supporting people with MS to maintain their social functioning, including their ability to work (e.g. Bevan et al., 2011).

Hakim and colleagues (2000) examined the social impact of MS using a population based survey in the UK. They found that 37% of respondents reported a decrease in their overall standard of living since diagnosis. Social withdrawal was related to severity of functional impairments, with more severely affected individuals reporting greater social isolation. One quarter of respondents reported that they had stopped visiting family and friends due to reduced mobility. Receiving a diagnosis of MS did not seem to affect marital status, with similar separation rates to the general population during the same period.

In terms of employment, 53% of those who were employed at diagnosis had given up their jobs, and those with more severe disability (as rated by the EDSS) were less likely to remain in employment. Respondents with RRMS were more likely to have remained in employment (70%) compared to those with secondary progressive MS (25%). Similarly Paltamaa's population survey found that 35% of people with MS of working age were currently working (Paltamaa et al., 2006). In terms of exploring the causal links between MS symptoms and change in employment status, Smith and Arnett (2005) report that the majority of people (85.7%) who are not working identified broad physical and neurological symptoms as the reason, while the majority (90%) of those who cut back their hours rated fatigue as the primary causal symptom. Interestingly, those still in work reported lower mood than those not working in this sample, which may relate to greater demands of being employed and lower perceptions of coping ability.

Some research has suggested that cognitive impairment, in addition to physical disability, has a substantial negative effect on social functioning and employment (e.g. Hakim et al., 2000; Honarmand et al., 2011; Rao et al.,

1991b). Benedict and colleagues (2006) report that several of the cognitive assessment measures are significantly related to employment status, in particular the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977) which specifically assesses auditory information processing speed and working memory. Another study found that, of the five variables which accounted for 49% of the variance in employment status, three were cognitive test scores; namely verbal fluency and two measures of verbal memory (Beatty et al, 1995). Other research has suggested that cognitive functioning, as measured by neuropsychological assessments, is unrelated to occupational status (e.g. Smith & Arnett, 2005). This study found no group differences in cognition between those who were working and those who were not. They noted that just over a quarter of unemployed people with MS mentioned cognitive impairment as a reason for the change in their employment status, much lower than the number of people who reported physical factors.

It may be that these mixed findings relate to heterogeneity in samples of people with MS, as well as the way in which cognitive functioning has been measured. One relevant factor might be the match between impaired abilities and the requirements of certain job types. For example, motor and mobility impairments may be more impairing for someone who has a manual job while someone working in an office may find cognitive changes more impairing (e.g. Chaytor, Schmitter-Edgecombe & Burr, 2006; Kornblith, La Rocca & Baum, 1986). The following section will consider cognitive impairments in MS in more detail.

1.4 Cognition in Multiple Sclerosis

1.4.1 Overview of Cognitive Changes and Variability in Presentations

Cognitive impairments in MS have increasingly been researched in the past two decades. The general consensus is that approximately half of all people

with MS display cognitive impairments if a comprehensive battery of neuropsychological tests is used for assessment and all clinical subtypes are included (between 40 and 65%; Amato et al., 2008). For example, 43% of a community sample of people with MS had impairments on four or more cognitive assessments (Rao et al., 1991a), with clinic samples typically displaying higher rates of impairment. Despite the frequency of cognitive difficulties, only a small minority have been found to have profound cognitive impairments and this is typically only seen in the more progressive disease subtypes (e.g. Guimarães & Sá, 2012). Neuropsychological performance is significantly correlated with magnetic resonance imaging (MRI) measured abnormality, specifically grey matter brain atrophy, ventricular enlargement and total cerebral lesion volume (Grassiot et al., 2009; Tiemann et al., 2009).

As with the other symptoms of MS, inter-individual differences in the cognitive impairments experienced are common, and not all people with MS display the same difficulties (Julian, 2011). This variability cannot be explained solely in terms of clinical course: cognitive impairments can be observed in all MS subtypes and in individuals who display little physical disability (Achiron & Barak, 2003; Amato et al., 2010). The emerging picture from the research to date is that impairments are observed even in the early stages of the disease and that these are likely to increase as the condition progresses, although some cognitive deficits can remain stable over time (e.g. Amato et al., 2001; Bergendal, Fredrikson & Almkvist, 2007). Furthermore, once cognitive impairments develop in MS they are unlikely to improve or remit, even when neurological symptoms may fluctuate (e.g. Bagert, Camplair & Bourdette, 2002).

In terms of disease subtype, Potagas and colleagues (2008) found that the prevalence of cognitive dysfunction increased from CIS (27.3%), to RRMS (40%) to SPMS (82.8%). This study found that 56.5% of the sample of people with PPMS, which is progressive from disease outset, met criteria for cognitive dysfunction. Considering RRMS on its own, Deloire and colleagues

(2005) investigated neuropsychological functioning in people who were newly diagnosed with RRMS, and found that 45% of their sample were cognitively impaired, which they defined as performance below the 5th percentile on two or more measures. More research is needed to fully understand the natural history of cognitive functioning in different subtypes and presentations of MS (e.g. Patti, 2009).

Where cognitive impairments are present, they are often associated with functional impairments, such as changes to employment (Amato et al., 2001), reduced medication adherence (Bruce et al., 2010) and reductions in driving safety (Marcotte et al, 2008). More recent reviews of the literature have suggested that, despite the heterogeneity in cognitive changes, a characteristic pattern of cognitive difficulties is associated with MS, and more specifically with subtypes of MS (e.g. Zakzanis, 2000). For example, a meta-analysis of 57 studies found that RRMS was associated with a moderate decline in cognitive functioning, with particular difficulties in "memory and learning" and "attention and executive functioning", the latter concepts here pertaining also to processing speed (Prakash et al., 2008). More recently, Ruet and colleagues (2013) found that PPMS was associated with much more pervasive cognitive difficulties when compared to the performance of matched controls (significant group differences were found on 70% of tasks administered), while impairments were much more specific in RRMS (significant group differences on 22% of tasks administered). The cognitive domains which have been found to be most impaired in MS are memory, information processing speed, attention, working memory and some components of executive functioning (Amato et al., 2010; Bobholz & Rao, 2003; Chiaravalloti & DeLuca, 2008; Julian, 2011).

1.4.2 Learning and Memory

Multiple sclerosis is associated with reductions in the ability to learn and recall new information. The prevalence rate of memory difficulties in MS has been

estimated to be up to 65% (Rao et al., 1993). Both verbal and visual explicit memory have been found to be impaired in MS, based on tasks such as word list learning and recall of object location on a grid (e.g. Zakzanis, 2000). Research suggests that implicit memory is intact in MS even when explicit memory is impaired (e.g. Seinelä et al., 2002). Much of the research on memory in MS has focused on anterograde memories, although there has been some suggestion of slightly reduced semantic remote memories also (e.g. Paul et al., 1997). McIntosh-Michaelis and colleagues (1991) examined everyday memory using a more ecologically valid measure of memory, the Rivermead Behavioural Memory Test (RBMT; Wilson, Cockburn & Baddeley, 1985) and found that 34% of their sample had total scores lower than one standard deviation below the normative mean.

Considering people with RRMS, the greatest memory impairments have been found to be on delayed recall of verbal information (large effect size), although difficulties have been noted for immediate verbal recall, as well as both immediate and delayed recall of visual information (medium effect sizes; Deloire et al., 2005; Prakash et al., 2008). Olivares and colleagues (2005) administered the Logical Memory subtests from the Wechsler Memory Scale Revised (WMS-R; Wechsler, 1987) and found that patients with early RRMS performed significantly poorer than control participants on immediate recall of verbal information, and this difficulty continued to be present for delayed recall. Fewer studies have investigated recognition memory. There is some evidence that recognition of verbal information is moderately impaired compared to healthy controls (Prakash et al., 2008), although other reviews have concluded recognition memory remains relatively intact (Zakzanis, 2000).

Earlier studies of memory in MS suggested that the retrieval of information was impaired in people with MS (e.g. Rao et al., 1989), but this has later been disputed (Thornton & Raz, 1997). More recently, explanations for poor memory have been based on inadequate acquisition of information during the

learning phase due to slowed information processing speed. Although individuals with MS tend to take more trials to learn information, they do not display problems recalling information that has been successfully encoded into memory (DeLuca, Barbieri-Berger & Johnson, 1994). Recall of short stories has also been found to significantly correlate with processing speed (Olivares et al., 2005). It is important to note that neuropsychological tests of memory often place demands on other domains such as attention and processing speed, as the information to be learned is briefly presented, and difficulties in these domains may also contribute to problems remembering information in everyday settings.

1.4.3 Information Processing Speed

Reduced speed of information processing has consistently been found to be one of the most robust cognitive impairments in people with MS, and has been linked with decreased neuronal conduction speed due to demyelination. DeLuca and colleagues (2004) found that 35.3% of their MS sample had impaired scores on the Processing Speed Index (PSI) of the Wechsler Adult Intelligence Scale Third Edition (WAIS-III; Wechsler, 1997), where impairment was defined as performance below the 5th percentile. Similarly, Drew and colleagues (2008) found that on average the PSI of the community sample of participants with MS was up to 10 points lower than their other index scores. If only participants with RRMS were considered, 21.6% of the sample showed impaired processing speed.

Two assessments of information processing speed have been frequently recommended for use with people with MS: the Paced Auditory Serial Attention Task (PASAT; Gronwall, 1977) and the Symbol Digits Modalities Test (SDMT; Smith, 1982). These measures have been associated with some of the highest effect sizes demonstrating cognitive impairment in people with MS. For example, one study reported that 57% of people with RRMS demonstrated impaired performance on either the SDMT or the PASAT, and

people with RRMS performed significantly worse on these measures compared to healthy control participants (Deloire et al., 2005). In this study, the SDMT was the most sensitive of all measures used (48% of RRMS participants performed below the 5th percentile on this measure). Information processing abilities have been found to be particularly strong predictors of longer term cognitive decline (Bergendal, Fredrikson & Almkvist, 2007).

One line of research has investigated whether slowed processing speed may be the 'primary' cognitive impairment in MS which results in difficulties in other cognitive process, such as learning briefly presented information. This hypothesis has been named the "Relative Consequence Model" (DeLuca et al., 2004). Slowed processing in MS has been correlated with poor verbal fluency, verbal working memory, and verbal and visuo-spatial memory, in addition to depressed mood and fatigue (Diamond et al., 2008). In keeping with this hypothesis, some research has found that if time constraints are removed, group differences in performance between people with MS and healthy controls become non-significant (Demaree et al., 1999). Research on this issue is inconclusive at present, although it is likely that processing speed deficits alone are not a sufficient explanation for the pattern of cognitive difficulties observed in MS (e.g. DeSonneville et al., 2002; Parmenter, Shucard & Shucard, 2007; Potagas et al., 2008).

1.4.4 Attention and Working Memory

Speed of information processing, attention and working memory, in addition to executive functioning, can be said to relate in that they involve the allocation of limited resources while completing cognitive tasks (e.g. Arnett, Higginson & Randolph, 2001). Many neuropsychological tasks place demands on more than one of these abilities and therefore it becomes important to explore these abilities in more detail. For example, the PASAT has been described as a measure of information processing speed, sustained and divided attention and working memory (e.g. Rogers & Panegyres, 2007).

From a neuropsychological perspective, attention has been described as a multifaceted concept, with several different assessments reflecting different constructs, such as selective attention, sustained attention, switching and divided attention plus several other executive measures of attention (e.g. Manly et al., 2001). Paul and colleagues (1998) report that the people with MS have preserved performance on automatic or low demand attention tasks, such as untimed visual cancellation tasks. As task demands increase, particularly if there is a significant speed, working memory or executive component, individuals with MS perform more poorly. Kujala and colleagues (1995) suggested that the poor performance of people with MS on attentional tasks may be best accounted for by cognitive slowness. The accuracy of the responses of people with MS is similar to that of healthy controls on some self paced tasks, despite slower performance, although higher executive demands may lead to higher error rates independent of processing speed (DeSonneville et al., 2002). In contrast, some studies have found people with MS to be impaired on simple and focused attention tasks, but these findings are often confounded; for example by motor reaction time response (e.g. Schulz et al., 2006).

There have been mixed results on the status of working memory abilities in MS, but it is generally accepted that working memory impairments are less common than processing speed difficulties. For instance, DeLuca and colleagues (2004) found that only 6.2% of their sample of people with RRMS had impaired scores on the Working Memory Index (WMI) of the WMS-III (compared to 21.6% on the PSI, see above). One suggestion is that as task demands increase, working memory difficulties become more pronounced for people with MS compared to controls. Parmenter and colleagues (2007) found that participants with MS took longer to respond as WM demands increased on a ‘n-back’ task. More complex tasks involving working memory, such as the PASAT (primarily a measure of processing speed; described

above), have consistently been found to be sensitive to impairments in people with MS even early in the disease (e.g. Landrø, Celius & Sletvold, 2004).

It is also possible that the probability of impaired working memory differs by MS subtype, with more advanced cases of MS being associated with greater WM deficits (DeLuca et al., 2004). For example, Zakzanis (2000) found only a small effect size overall for Digit Span measures, and this was lower for the RRMS compared to the more progressive groups. Furthermore, Ruet and colleagues (2013) found that while PPMS was associated with impairments on digit span, RRMS was not. Similarly, one study found that Digit Span performance was unimpaired in people with predominantly RRMS (90% of sample; Rendell, Jensen & Henry, 2007) while another study found that Digit Span was impaired when a group of mixed MS subtypes (41% RRMS) was compared to normal controls (Paul et al., 1998).

In summary, it is likely that the status of attention and working memory abilities in MS is complex. MS is not associated with consistent impairments in these abilities but several factors increase the likelihood of impairments including level of task demands, nature of the demands (e.g. time pressure, executive processing) and the subtype of MS in question.

1.4.5 Executive Functioning

Executive functioning refers to the use of higher level cognitive abilities involved in the control and regulation of lower level cognitive processes (such as attention, memory, language) in order to work towards a future goal (Alvarez & Emory, 2006). These executive processes include planning, problem solving, abstract thinking, inhibition, initiation, set shifting and monitoring performance; with many of these functions also drawing on working memory and attention abilities. Novel and unfamiliar tasks and situations typically have higher executive demands than routine ones. Many of

these higher level processes have been linked to the prefrontal cortex, although other brain regions are also involved (Alvarez & Emory, 2006).

Structural brain imaging research in MS has suggested that, while MS can affect any part of the CNS and brain, there is a higher probability that lesions will affect the frontal, as well as the temporal and parietal lobes of the brain in the early stage of the disease (Pirko et al., 2002; Sailer et al., 2003; Sperling et al., 2001). There has also been some evidence that frontal cortex atrophy predicts some forms of cognitive impairments in MS (Benedict et al., 2002). In keeping with this prediction, both clinical and empirical descriptions of executive dysfunction have been reported in the literature (e.g. Rao et al., 1993). Research on executive functioning in MS will be described in detail below.

In terms of the prevalence of executive dysfunction in MS, Godefrey and colleagues (2010) administered seven commonly used executive measures to a group of people with MS referred for a cognitive assessment. They found that 28% of the sample displayed performance consistent with cognitive dysexecutive syndrome, defined as performance below the 5th percentile on 3 or more tasks. Behavioural dysexecutive syndrome (identified via a semi-structured interview with an informant) was higher, affecting 38% of the sample. These authors note that initiation difficulties were most common in MS, although as simple reaction time was not controlled for this may have been due to slowed processing speed.

Drew and colleagues (2008) administered the Delis-Kaplin Executive Functioning System (D-KEFS; Delis, Kaplan & Kramer, 2001) to a mixed community sample of 95 people with MS (50% of whom had RRMS). The findings of Drew's study will be used throughout this section to give an estimate of the prevalence of different types of executive difficulties; however it should be noted that a relatively liberal definition of impairment was used (one standard deviation below the normative mean). In this sample the status

of executive functioning was heterogeneous. Approximately one third of participants (34%) showed no difficulties on the tasks, with 17% performing in the 'impaired' range on six or more measures. The tasks with the poorest performance all included a timed component, and as motor and cognitive slowing was not accounting for, the results may in part reflect difficulties in lower level processes associated with MS. More generally, the areas of executive functioning most researched in the literature include: verbal fluency, inhibition, planning, prospective memory, set shifting and divided attention (e.g. Guimarães & Sá, 2012)

1.4.5.1 Verbal Fluency

Verbal fluency tasks are typically considered assessments of executive functioning and language. The executive component involves generation of words within a limited amount of time, and use of strategy to optimise performance efficiency (e.g. Henry & Crawford, 2004). Verbal fluency tasks are divided into 'Category Fluency', which involves generating words from specific semantic categories, and 'Letter Fluency', which involves generating words beginning with particular letters (also called phonetic fluency). Some measures also include a further switching component, which involves alternating between generating words from two categories. One of the most commonly used measures of verbal fluency is the Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1976). In Drew's (2008) study, verbal fluency was one of the most commonly impaired abilities: 27% of the sample showed reduced performance on the switching subtest of the D-KEFS fluency task, while 22% and 16% had poor performance on the letter and category fluency, respectively.

Henry and Beatty (2006) conducted a meta-analysis of verbal fluency research in MS, and concluded that MS is associated with a substantial impairment in both letter and category fluency, which is larger than that seen for other measures of executive functioning. However, the authors suggest that this impaired performance may be in part explained by slowed

information processing, as the fluency effects were equivalent to or less than deficits on information processing tasks like the SDMT. On the other hand, it may be that tasks like the SDMT also have an executive component, meaning that part of the impairment observed on both these tasks may reflect difficulties with executive demands. Zakzanis (2000) conducted an earlier meta-analysis and concluded that verbal fluency deficits were found in MS, but that impairments in category fluency were greater than in letter fluency; a pattern which suggests that this may partly relate to reduced language abilities.

With regard to MS subtype, both reviews noted that RRMS was associated with fewer verbal fluency deficits than progressive forms of MS, but this may be explained by age and disability, rather than subtype *per se* (Henry & Beatty, 2006). Amato and colleagues (2001) note that verbal fluency impairments were not observed shortly after diagnosis in their sample, but were apparent 4.5 years later. Prakash and colleagues (2008) reported that verbal fluency measures are amongst the most sensitive of the commonly used measures of executive functioning in RRMS, resulting in medium/large effect sizes.

1.4.5.2 Inhibition

Inhibition refers to the suppression of a habitual response or a context-inappropriate response (e.g. Burgess & Shallice, 1998). Neuropsychological assessments which are postulated to measure inhibition include the Stroop test (Stroop, 1935), in which participants are asked to name the ink colour that words are printed in while ignoring what the word reads, and section two of the Hayling Sentence Completion Task (Burgess & Shallice, 1997), in which participants are asked to provide a semantically unconnected word to complete unfinished sentences. Both of these tasks measure response time, with the assumption that longer response latencies and more errors indicate greater difficulty inhibiting previously learned responses. A recent study of a mixed group of participants with MS reported that 17.6% of the sample

performed 1.5 standard deviations below the control mean on the Stroop task (Feinstein, Lapshin & O'Connor, 2012). Drew and colleagues (2008) found that the Colour Word Interference task (similar to the Stroop task) was the second-to-most impaired task administered, with 25% of MS participants performing one standard deviation below the normative mean for the inhibition trial. One study used the Hayling test with people with MS and found that 10% of the sample was impaired, defined as performance below the 5th percentile of normative data (Summers et al., 2008).

In terms of RRMS specifically, the Stroop test has been found to be one of the most sensitive of the commonly used measures based on a meta-analysis (Prakash et al., 2005). One study reported that 36% of their sample was impaired on a computerised version of the Stroop (requiring a verbal response), with the RRMS group performing significantly worse than matched controls (Deloire et al., 2005). However, the same sample was unimpaired on another test of inhibitory function, the go-no go paradigm (requiring a motor response) and no interpretation of this discrepancy was provided.

One difficulty in interpreting these results is that the most commonly used measures of inhibition involve reaction time, and so the reduced performance of people with MS may be partly attributable to impaired processing speed rather than executive dysfunction alone. Two studies have examined this issue and found that people with MS were slower on the 'low level' comparison trials of the Stroop (word reading and colour naming); in addition to the inhibition trial (Denney et al., 2003; MacNiven et al., 2008) with the suggestion that this overall profile is more in keeping with slowed information processing.

This is not to say that there impaired Stroop performance in MS does not also involve executive dysfunction. One recent study reported evidence that some people with MS find it difficult to screen out information not relevant for the task at hand, a trait referred to as 'inattentional blindness', commonly

observed in healthy control participants. While this study found no overall group differences in distractibility the authors noted that a subset of people with MS, namely those with impaired performance on the Stroop and PASAT tasks, may become more easily distracted and experience difficulty screening out task irrelevant information. The authors suggest this may contribute to workplace inefficiency and difficulties with multitasking (Feinstein et al., 2012).

1.4.5.3 Planning

Planning can be defined as the generation, selection and evaluation of a sequence of actions to achieve a desired goal, and is felt to be particularly important in navigating novel situations efficiently. The most frequently used neuropsychological measures of planning in MS are the Tower of Hanoi and related tasks (Tower of London, Tower task of the D-KEFS). These tasks involve participants moving objects from one position to another, following certain rules, with instructions to achieve the goal in as few moves as possible.

Results from a community sample suggest that the total score from the Tower Task was less sensitive to cognitive difficulties in MS compared to other executive measures, with 13% of the sample showing reduced performance (Drew et al., 2008). Foong and colleagues (1997) found that, once motor response speed was controlled for, people with MS (predominantly SPMS) were slower only for the most demanding trials of the task. However, they found that participants were less efficient throughout the trials, taking more moves to solve all trials and solving fewer trials in the minimum number of moves. Arnett and colleagues (1997) found that people with MS spent significantly longer to plan each move and they also solved fewer trials, although they imposed a two minute time limit per trial. Another study found that while a group with predominantly RRMS was associated with longer planning times (pauses before making an initial move), there was no difference in accuracy between groups (Denney et al., 2004). Low mood and

depression has also been linked to significantly poorer performance on this task (Arnett, Higginson & Randolph, 2001).

1.4.5.4 Prospective Memory

A small number of studies have examined the status of prospective memory, also referred to as delayed intentions or memory to do something in the future, in people with MS. Rendell and colleagues carried out detailed studies of this ability, using an experimental task which simulates a calendar week (the 'Virtual Week'; Rendell et al., 2007; Rendell et al., 2012). They report that people with predominantly RRMS have impaired prospective memory regardless of task demands; this finding was true for both routine and occasional tasks, whether these were prompted by time or a specific event, and whether they were related to the current task or not. The majority of errors were 'misses' where participants had no recall of having to carry out an action (prospective component), rather than simply forgetting what they had to do (retrospective component). Other studies have found similar findings, with the suggestion that failures in prospective memory are more likely to occur on more resource demanding and novel tasks compared to relatively routine and automatic tasks (Kardiasmenos et al., 2008).

1.4.5.5 Set Shifting and Cognitive Flexibility

Set shifting refers to the ability to display cognitive flexibility, for example switching between activities or responses in line with a desired goal. Difficulties in this ability can lead to perseveration, where a particular action or response is made repeatedly despite changing circumstances. One of the most commonly used assessments of executive functioning in MS is the Wisconsin Card Sorting Task (WCST; Heaton et al., 1993), which is felt to primarily tap into the ability to set shift. Drew and colleagues (2008) reported that between 12% and 15% of their community sample performed poorly on a card sorting task.

Zakzanis (2000) reported that, when combining results from all MS subtypes, the effect sizes for different outcome variables from the WCST fell in the medium range. However, comparing progressive subtypes and RRMS, they note that WCST preservative errors were sensitive to the impairments in progressive MS only. In contrast, Denney and colleagues (2004) found that participants with MS performed significantly worse than control participants, and there was no difference between RRMS and PPMS participants. Other studies have noted that WCST performance tends to be less sensitive to cognitive difficulties than other executive tests such as verbal fluency (e.g. Prakash et al., 2008; Henry & Beatty, 2006).

1.4.5.6 Divided Attention & Multitasking

One aspect of executive functioning relates to dividing cognitive and attentional resources between competing demands. This can involve alternating attention between two tasks (as in the Trail Making Test; TMT; Reitan & Wolfson, 1985) or completing several tasks over time (as in the Six Elements Test; SET; Shallice & Burgess, 1991). It can also involve performing two tasks simultaneously (as measured by tasks such as the Dual Task Paradigm; Della Sala et al., 1995). One of the most commonly used measures is the TMT and variants. Drew and colleagues (2008) found that Trail Making was one of the most sensitive measures included in the D-KEFS, with 23% of the sample performing poorly on this measure. In contrast, Zakzanis (2000) cautions that the TMT Part B is less sensitive to the executive difficulties associated with MS compared to other tasks, with 71% overlap between the performance of cases and controls.

De Sonneville and colleagues (2002) investigated various attentional domains, and found that divided attention was most impaired for people with MS in more complex tasks, and specifically that there was a disproportionate reduction in processing speed when task demands involved switching between two attentional sets. They reported that RRMS participants performed worse than controls, with no differences observed between MS

subtypes. In terms of dual task performance, one study investigated whether performing two relatively undemanding tasks (e.g. judgement of line orientation and humming a learned melody) concurrently would lead to a disproportionate performance decrement compared to performing them singly (D'Esposito et al., 1996). This study found that MS was associated with a dual task decrement only for more demanding tasks (i.e. humming a melody, reciting the alphabet), but not finger tapping, which they interpreted as evidence of limited central executive functioning.

To our knowledge, no published study has reported specific details of the performance of people with MS on multitasking tasks such as the SET.

1.4.5.7 Summary of Executive Functioning in Multiple Sclerosis

In summary, the current literature suggests that MS is associated with deficits on many tasks assumed to measure executive functioning, including measures of verbal fluency, inhibition and distractibility, planning, prospective memory, set shifting and divided attention. Verbal fluency and inhibition tasks such as the Stroop have been found to be particularly sensitive to cognitive dysfunction in MS. However, it is less clear whether poor performance on these tasks is attributable to executive dysfunction, impairments in lower level processes such as processing speed, or a combination of the two. If the latter is the case, it is unclear what the relative contribution of these factors is. Nonetheless, the most probable interpretation is that both executive and lower level process deficits contribute to the observed performance of people with MS, as performance typically reduces as executive demands increase.

One difficulty is that many tasks rely on differences in response time to infer difficulties with executive demands. A different approach would be to use tasks that simulate more realistic situations, and to measure multiple measures of performance to gather more information on these questions.

1.4.6 Other Cognitive Domains

Research on the status of other cognitive abilities in MS generally suggests that these are relatively intact. In terms of general intellectual functioning, research has suggested that, at a group level, there is a slight decrease in full scale intelligence quotient (FSIQ), which is mostly accounted for by decreased performance on processing speed and timed tasks reflected in a greater reduction in 'performance' indices compared to verbal indices (e.g. Drew et al., 2008). More commonly, research has noted a slightly greater discrepancy between predicted and actual IQ scores.

Language abilities have typically been shown to be preserved in adults with MS, although there may be some subtle difficulties caused by reduced speed of information processing, such as in sentence completion (e.g. Amato, Zipoli & Portaccio, 2008; Bergendal et al., 2007; Langdon, 2011). Visuospatial abilities tend to be relatively preserved in earlier stages of MS (e.g. Prakash et al., 2008). Some reviewers note mixed results for visuospatial abilities, although it is possible that these abilities are increasingly impacted as the disease continues (Amato et al., 2008; Winkelmann et al., 2007).

1.4.7 Impact of Non-Cognitive Factors on Cognition

In people with MS, cognitive impairments are likely to coexist with other factors which impact on everyday cognitive functioning, such as fatigue, depression and apathy. It is important to consider whether these factors can affect performance on neuropsychological assessments.

1.4.7.1 Low Mood

Depression is one of the most studied of these factors, and while findings have been mixed, it is likely that there is a positive correlation between depression and cognitive dysfunction in MS when higher quality studies are considered (Arnett, Barwick & Beeney, 2008). One study identified low mood (and other forms of negative affect such as anxiety) as a predictive factor for

subsequent cognitive impairment in MS (Christodoulou et al., 2009), particularly with regard to memory for newly learned information. Other longitudinal studies have reported that the influence of depression on cognitive functioning depends on how cognition is measured. Several studies have found that depression may correlate with subjective reports of cognitive functioning, but this association is not observed between depression and performance on neuropsychological assessments (Julian, Merlizzi & Mohr, 2007; Kingsinger, Lattie & Mohr, 2010). Similarly, other authors have found no correlation between neuropsychological performance and self rated depression (e.g. Potagas et al., 2008).

1.4.7.2 Apathy

While it is likely that depression and apathy overlap to a large degree, apathy may also arise from dysexecutive syndrome and thus theoretically can be observed independent of depression. One study has considered associations between apathy (as measured by the Frontal Systems Behaviour Scale – FrSBe; Grace, Stout & Malloy, 1999) and a brief battery of neuropsychological assessments (Chiaravalloti & DeLuca, 2003). This study found that self and family reports on the behavioural indices of apathy correlated with more effortful cognitive tasks including higher order executive functions as measured by semantic fluency, digit span backwards and PASAT, and noted that elevated apathy was reported by half of their sample of patients with MS.

1.4.7.3 Fatigue

Fatigue is commonly reported by patients with MS, with up to 90% of people reporting this problem (Schapiro, 2002). While the general consensus from the literature is that there is no association between subjective reports of fatigue and poor neuropsychological task performance, patients with MS tend to perform poorly on tasks thought to be sensitive to the effects of fatigue, such as those that require sustained mental effort (Chiaravalloti & DeLuca, 2008). Krupp and Elkins (2000) found that, when a neuropsychological battery was administered twice in a single four hour session, with a sustained

continuous cognitive effort task between administrations, the performance of people with MS decreased on the second administration. In contrast, healthy control participants showed improved performance on repeating the tasks, despite both groups reporting subjective fatigue. The subtests most impacted were considered to be more demanding, for example verbal memory and planning.

1.4.8 Summary of Cognitive Profile in MS

In summary then, the cognitive domains most affected by MS include speed of information processing, explicit memory, executive functioning and more complex and demanding tasks assessing attention and working memory. One of the complexities of MS research is the heterogeneity of cognitive performance, ranging from pervasive difficulties across several domains to no evidence of cognitive impairment. This is increasingly being understood in terms of a combination of the type and location of structural brain changes, the time since symptoms of MS first occurred and the prognostic subtype of MS in question. Another difficulty in this area of research involves partitioning out the effects of lower and higher level abilities, in particular as speed of information processing deficits can have an impact on many different neuropsychological and everyday cognitive tasks.

To date, most research on cognition in MS has made use of traditional measures of cognitive domains. A complimentary approach to cognitive assessment is to use more ecologically valid measures which have been developed to more accurately simulate and predict performance in everyday activities, to gather further information on the status of cognition in MS. This approach will be outlined below, with a particular focus on executive functioning.

1.5 Assessments of Executive Functioning

1.5.1 Limitations of Traditional Neuropsychological Measures

Chaytor and Schmiter-Edgecombe (2003) note neuropsychological assessments were historically often developed and used to assist diagnosis, by attempting to identify brain pathology. Thus these assessments aimed to ascertain what an individual can do: their optimal performance. Traditional neuropsychological measures involve completion of tasks which are designed to isolate performance on one or more cognitive domains, while controlling for other factors such as environment. Tasks are typically short and novel, with clear rules and instructions, and a single well defined goal. Administration involves individual attention from an experimenter, little or no feedback on performance, minimal environmental distractions and prompts to initiate and stop tasks. The use of compensatory strategies, such as writing information down to aid memory, is generally restricted (e.g. Chaytor et al., 2006; Sbordone, 1996). These testing conditions allow for the effects of confounding factors to be minimised, and to increase the likelihood that observed performance accurately reflects the person's ability in the target cognitive domain(s).

As brain imaging techniques have developed, and have been able specify localised brain pathology, the neurobiological diagnostic role of neuropsychological procedures has decreased drastically. Simultaneously, neuropsychological tests were more frequently being requested to comment on areas of everyday cognitive functioning, such as educational and occupational functioning, as well as the potential for rehabilitation. Chaytor and Schmiter-Edgecombe (2003) note while the use of these neuropsychological tasks has changed, many of the most widely used tests have remained the same. This opens the possibility that traditional neuropsychological assessments may not be ideally suited to provide information on everyday functioning, which involves assessing what

individuals actually do in real world settings (rather than what they can do). This is termed ecological validity: the degree to which assessments are able to predict performance of patients in everyday life (Wilson, 1993).

Within this context, it may be that some of the desirable conditions in assessing optimal functioning may confound assessments of everyday functioning. Several other limitations of traditional neuropsychological tests have been noted in this regard also. Heinrichs (1990) notes that traditional measures may be too abstract and general to reflect skills relevant for everyday settings and that these tasks do not consider the role of environment in creating disability. Traditional neuropsychological tasks may also fail to take account of non-cognitive factors which contribute to everyday performance, such as motivation, personality, physical illness, social support and personal history (Chaytor et al., 2006; Wilson, 1993). MacNiven and colleagues (2008) note that there is lack of agreement on what traditional tests such as the Stroop actually measure.

These limitations are particularly problematic for a disease with wide ranging effects, such as MS. Furthermore, as cognitive deficits in MS are thought to be more pronounced during complex and demanding activities, traditional neuropsychological tasks may not be sensitive to the types of cognitive dysfunction associated with MS. This complexity may be more characteristic of real world environments, such as the workplace, highlighting the potential benefits of assessing more everyday cognitive abilities. Nonetheless, these approaches can be seen as complimentary: there are benefits to using assessments of both optimal performance in circumscribed cognitive domains and assessments which predict everyday cognitive functioning together in order to further our understanding of cognitive difficulties in MS.

1.5.2 Ecologically Valid Measures

With regard to adapting neuropsychology to the assessment of everyday functioning, Franzen and Wilhelm (1996) delineate two separate approaches. The *veridicality* approach involves investigating the degree to which existing neuropsychological assessments are related to measures of everyday functioning. Within this approach, a number of decisions are important, for example which area of everyday functioning is used for comparison, what outcome measures are used and what sources of information are drawn upon. Traditional neuropsychological measures of executive functioning have most commonly been found to explain a moderate amount of variance in everyday functioning. For instance, one study reported that the combined predictive power of the COWAT, TMT, Stroop and WCST tests explained approximately 20% of the variance in everyday functioning, as rated on informant report questionnaire (Chaytor et al., 2006).

On the other hand, it is also important to clarify what is meant by the term "everyday cognitive tasks". Research on the ecological validity of traditional neuropsychological assessments has been mixed, with the suggestion that ecological validity varies by population and the way in which everyday functioning is measured. Typically, these studies have focused on prediction of activities of daily living (ADLs; physical self maintenance tasks) and employment status (Chaytor & Schmiter-Edgecombe, 2003). It could be argued that these activities vary in relation to how cognitively demanding they are, with some activities having relatively few cognitive demands. Further research in this area is needed, which compares neuropsychological test performance to performance on a wider range of more demanding everyday activities using different sources of information. For instance, one study found that neuropsychological test results in people with early dementia correlated with instrumental activities of daily living (IADLS; more complex self maintenance tasks including using the telephone, managing finances and medications), but not ADLs (Barberger-Gatau et al., 1999).

Verisimilitude refers to the degree to which the cognitive demands of an assessment task theoretically resemble the demands of an everyday cognitive task in a real world environment (Franzen & Wilhelm, 1996). Neuropsychological tasks developed using the verisimilitude approach tend to focus on how much face validity the assessment has, rather than how well the task differentiates between groups. Typically, this has involved the development of new tasks over the past two decades. Examples include the Test of Everyday Attention (TEA; Robertson et al., 1996) and the RBMT. These tasks include activities such as searching maps, counting elevator tones, remembering people's names and remembering to ask the experimenter to return objects they put away at the start of the assessment. One study examined the ability of the TEA and RBMT to predict functional status in a mixed sample of people with MS (Higginson, Arnett & Voss, 2000). The findings indicated that these measures were better predictors of functional disability than traditional measures and questionnaires. An additional advantage of these more ecologically valid tasks is that successful rehabilitation would be expected to improve performance, even though there may be no change in brain pathology.

Ecologically valid tests of executive functioning have tended to take two forms: (1) real world tasks were participants are observed in an everyday setting, such as in the Multiple Errands Task (MET; Shallice and Burgess, 1991) and (2) tasks which aim to simulate real world activities in the laboratory or clinic, such as the subtests of Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson et al., 1996) and the Hotel Task (Manly et al., 2002). The sensitivity of these measures to the cognitive abilities of people with MS has rarely been investigated.

Considering these more ecologically valid tasks in the greater detail, the MET is conducted on a shopping street or hospital ward, and therefore is not easily administered alongside a traditional, clinic based neuropsychological battery. In contrast, the Six Elements Task (SET; Burgess & Shallice, 1991) included

within BADS was developed to be administered in a standard clinic setting. This task involves completing some of three different tasks, divided into halves, over the space of ten minutes and while following certain rules. Participants are informed that they will not have time to complete all the tasks, and so must monitor their time and switch between incomplete tasks in order to follow the instructions. However, it could be argued that the activities within the SET (dictation, arithmetic and picture naming) have relatively low cognitive demands and are not fully representative of the types of cognitive tasks people typically carry out on a daily basis. The Hotel Task was developed as a modification of the SET task, and involves performing more demanding activities associated with administrative tasks often required in the workplace. The following section will consider the Hotel Task in more detail.

1.5.3 The Hotel Task

In the Hotel Task, participants are asked to complete some of each of five different activities in 15 minutes, spending equal time on each, and also to remember to press a button twice at predefined times. As participants are told that they have insufficient time to complete the activities fully, the use of planning and divided attention abilities are needed in order to successfully achieve the overall task goal. Like the SET, the Hotel Task requires participants to monitor the time and their progress towards the task goals to perform the task successfully. This task places demands on set shifting ability, as participants must move from one activity to another without external cues (such as being prompted or completing the subtest), in order to follow the task instructions. In addition, the Hotel task includes a test of prospective memory, in that participants are instructed at the beginning of the task to remember to press buttons at specified times. As such, participants are faced with multiple goals and distractions within the task, have fewer prompts to begin and finish activities and are required to manage their own time over a 15 minute period. Furthermore, the Hotel Task can be said to have more face validity than traditional tests of executive functioning, in that it involves activities that would

plausibly be completed while working in an administrative role in a hotel or business.

Manly and colleagues (2002) reported that the Hotel Task is sensitive to executive dysfunction in everyday life (as rated by informant report) and that this is true even when performance on the SET was not substantially impaired. Only one published study has administered the Hotel Task to a small sample of people with RRMS and healthy controls, in the context of a brain imaging study (Roca et al., 2008). They found that the group with RRMS were not impaired on traditional measures of executive functioning (TMT, WCST, verbal fluency) but did display some impairments on the Hotel Task, the MET and other more ecologically valid tests. Specifically, deficits were found in the prospective memory component of the Hotel Task, as well as planning and organisation in the MET, as indexed by "task failures" (not completing a task) and "Interpretation failures" (not understanding or following instructions correctly). This study provides some preliminary evidence of the possible utility of more ecologically valid tests of executive functioning in people with MS.

1.6 The Current Study

1.6.1 Summary of Study Rationale

In summary, MS is a disease affecting the brain and CNS which can cause a wide range of symptoms across several domains: physical, emotional and cognitive. These symptoms interact and lead to varying levels of disability, for example impacting on social and occupational functioning. Over the past two decades, a substantial number of empirical studies have been carried out investigating the status of cognitive abilities in MS. The findings have generally been mixed, although progress towards identifying a characteristic pattern of cognitive difficulties in MS has been made using traditional neuropsychological tasks. There have been mixed findings about whether

poor performance on traditional neuropsychological tasks predicts impairments in everyday cognitive functioning, such as employment difficulties. One complimentary method of assessment, the use of more ecologically valid assessment tasks, may provide further information on the everyday cognitive difficulties reported by people with MS.

1.6.2 Aims

The current study aimed to investigate the performance of people with MS on the Hotel Task, a more ecologically valid test of executive functioning. Previous studies have been criticised for combining different MS subtypes within a single research sample, despite evidence of differential patterns of impairment (e.g. Zakzanis, 2000). Accordingly, the current study investigated cognitive performance in RRMS only. The Hotel Task was administered to a group of people with RRMS and matched healthy control participants, alongside traditional assessments of cognition. Questionnaire measures of other relevant factors, such as mood, fatigue and apathy, were also administered. The primary aim of the study was to ascertain whether the Hotel Task is more sensitive than traditional measures to the cognitive deficits associated with MS.

In order to investigate the relative contributions of higher level executive impairments (e.g. impaired planning and set shifting) and lower level impairments (e.g. reduced information processing speed), a modified version of the Hotel Task was additionally administered to participants. This modification was inspired by other executive tasks which seek to compare performance on high and low executive demand versions of the same task. One such assessment task is the Zoo Map subtest of the BADS. The high demand condition of this task requires participants to plan and plot a route through a map while following certain rules. The low demand condition requires the participant to follow a route specified by the examiner through a map. If participants are disproportionally impaired on the high demand version

of this task, this provides evidence of executive dysfunction. If participants perform poorly on both conditions, it may be that more pervasive difficulties are present.

In the current study, the Hotel Task was administered to participants twice. The first administration replicated the conditions of the original Hotel Task. In order to gather more information on the relative contribution of executive functioning to the performance of participants on the Hotel Task, a novel second condition was developed. This second administration reduced the executive demands of the task by providing participants with a pre-defined plan to optimise performance on the task, along with verbal prompts to switch between activities at the appropriate times. The goal of this additional condition was to gather data on the performance of participants on the component activities when they were not required to also multitask, generate and implement a plan, switch tasks without external prompts, monitor time and remember to perform actions in the future. Should participants with RRMS have a disproportionate difficulty with these aspects of executive functioning; it was hypothesised that they would display a disproportionate impairment on the high executive demand version of the Hotel Task relative to this novel 'low demand' second condition, when compared to a group of people without RRMS,. A further adaptation to the original task involved recording the actual performance of participants on each component activity, in addition to the degree to which participants followed the instructions. Comparing these outcome measures provided further information on whether any deficits are due to features of executive dysfunction, or rather reduced abilities more generally.

Throughout the following sections, 'executive functioning' will refer to the abilities thought to be required to successfully and efficiently complete the Hotel task, including aspects of multitasking and divided attention, planning, inhibition, switching, monitoring and prospective memory. This is for the sake

of brevity, and it is acknowledged that other abilities are also included in the category of executive functions more generally.

1.6.3 Hypotheses

The following main predictions were made:

1. Participants with RRMS will perform poorly in terms of the executive variables on the high demand (Standard) condition of the Hotel Task relative to healthy control participants, if executive abilities are compromised in RRMS.
2. Participants with RRMS will show fewer deficits on the main Hotel Task variables in the lower executive (Structured) version of the Hotel Task, compared to the Standard version.
3. Participants with RRMS will demonstrate reduced performance efficiency on both conditions of the Hotel Task compared to controls, reflecting lower level cognitive impairments such as slowed information processing speed.
4. Performance on the Hotel Task will demonstrate greater sensitivity to the cognitive difficulties experienced by people with RRMS compared to traditional measures of executive functioning.

In addition, the two secondary hypotheses explored were:

5. Neuropsychological task impairments will remain significant when symptoms of depression, fatigue and apathy are statistically controlled for.
6. Hotel Task performance will be associated with cognitive difficulties in daily life, as indexed by self reported executive dysfunction and informant rated instrumental activities of daily living.

2 Method

2.1 Ethical Approval

Ethical approval for this study was given by the London – Dulwich Research Ethics Committee (REC reference: 12/LO/1306; see Appendix 1).

2.2 Design

The executive performance of participants on the standard condition of the Hotel task (time deviations, number of tasks completed, clock checks) was examined by comparing independent group means (RRMS vs. Control). Where data were normally distributed, performance efficiency across conditions was compared in a 2 (Group: RRMS vs. Control) x 2 (Condition: standard vs. structured administration of the Hotel Task) mixed model multi-factorial design, with group as the between subjects factor and condition as the within subjects factor. Where data did not meet the assumptions of parametric analyses, non-parametric tests were carried out comparing the difference across conditions for each group.

Group differences on a selection of traditional neuropsychological tasks and questionnaires were analysed by comparing group means (RRMS vs. Control). The sensitivity of the Hotel Task to cognitive dysfunction was examined through comparison of clinical impairment levels across tasks, as defined by reduced performance compared to healthy control participants. The association between neuropsychological performance variables and questionnaire variables was examined by calculating the regression coefficient using an ANCOVA analysis (where parametric analyses were appropriate) and by using Spearman's Rho analysis (when parametric analyses were not possible).

2.3 Participants and Recruitment Procedure

2.3.1 Sample Size

Power analysis was based on one previous study that has used the Hotel Task with a sample of people with RRMS (Roca et al., 2008). This study examined the performance of people with RRMS on tasks of cognitive function, including the Hotel Task, in addition to neurological changes as detected using diffusion tensor imaging. This study had a small sample size (n = 12 in each of the two groups). Using the data from the participants in this study, a power analysis was conducted using nQuery Advisor version 4.0. Roca and colleagues found that the 'Button Deviation Times' (i.e. the degree to which the time that participants pressed a button deviated from the optimal time) significantly differed between groups. Participants in the RRMS group had a mean deviation of 6.92 seconds and participants in the control group had a mean deviation of 5.08 seconds. The common standard deviation was calculated to be 2.17 seconds, giving an effect size (*d*) of .847. A two sample t-test indicated that a sample size of 23 participants in each group would be required to detect a between-subjects difference in 'Button Deviation Times' of this size with 80% power and an alpha level of 0.05.

2.3.2 Groups

2.3.2.1 Clinical Group: Relapsing Remitting Multiple Sclerosis

Twenty participants with a clinical diagnosis of RRMS were recruited to take part in the study from the Queen Elizabeth Hospital, South London Healthcare NHS Trust (SLH). The participant with the lowest estimated general cognitive functioning was excluded in order to improve the matching of group demographic variables, leaving 19 participants. Participants were given a research information pack, which included the Participant Information Sheets for participants with MS and informants as well as an introductory letter from their neurologist (Appendix 2), and were asked by their clinician (Consultant Neurologist or MS Nurse) whether the author could discuss the research with them. Potential participants who agreed were approached by the principle

investigator and provided with verbal information about the study, as well as the opportunity to ask questions. Those who agreed to take part were screened using a short interview to determine whether they met the inclusion criteria.

Participants were included in this group only if they had an existing diagnosis of MS in line with the revised McDonald criteria (Polman et al., 2010) with a relapsing remitting disease course, were of working age (18 to 65 years old), were fluent in English and had the ability to give informed consent.

The exclusion criteria for this group included severe cognitive impairment (e.g. dementia), any other neurological or major medical condition likely to affect cognitive performance, medication usage likely to affect cognitive performance, a diagnosis of a major psychiatric disorder, a diagnosis of alcohol or substance abuse, fatigue or disability of a degree which would make it impossible to complete the assessments and relapse in symptoms during the four weeks prior to the testing session.

An appointment to complete the research protocol was arranged with these participants. This appointment took place either in a clinic room at the Queen Elizabeth Hospital (n = 16) or in their own homes (n = 2), and one participant completed the assessment at a laboratory at the Institute of Psychiatry (n = 1). Three potential participants expressed interest in taking part in the research, but later decided not to carry out the research session.

2.3.2.2 Informants

Participants were asked to nominate an informant (a family member or someone who knows them well), to complete two questionnaires, either in person (if they attended the research appointment) or via post. The relationship of the informant to the person with RRMS was described as follows: partner (n = 10), parent (n = 5), sibling (n = 1) and child (n = 1). One participant reported that no one knew them well enough and returned the

blank questionnaires, and one participant did not return the questionnaires via post despite reminders.

2.3.2.3 Control Group: Healthy Controls

Twenty participants were recruited from the community. The participant with the highest estimated general cognitive functioning was excluded for matching purposes, leaving 19 participants. Participants were recruited through online community forums (n = 14) as well as a participant database maintained by King's College London (n = 5). Potential participants who responded to the research listing on the online community forums were contacted to complete a brief screening procedure before being invited to take part in the study. Lists of potential participants from the participant database were obtained, and these were used to select volunteers who closely match the participants in the RRMS group in terms of age, gender and years of education. Potential participants from all sources who were found to be appropriate for the study were sent the participant information sheet (Appendix 3) by email, and were given the opportunity to consider whether they would like to participate, as well as to ask questions. Those who agreed to take part completed all tasks and questionnaires during a single research session. The exclusion criteria for this group were similar to the criteria for the RRMS group.

The appointments for 18 healthy control participants took place at a laboratory at the Institute of Psychiatry and one participant was assessed at their own home. Six potential participants, who met the inclusion criteria and expressed interest in participating in the research, later decided not to take part and did not complete the research session.

2.4 Measures

2.4.1 Ecologically Valid Executive Functioning Task

The Hotel Task (Manly et al., 2002) was designed to capture the features of complex, everyday cognitive activities, in this case activities that would

plausibly need to be completed in the course of running a hotel. Participants were asked to carry out as much of each of six activities as they could in 15 minutes, spending an equal amount of time on each activity. The activities included (1) calculating individual bills, (2) categorising and sorting coins in a money box, (3) finding phone numbers in a telephone directory, (4) sorting name labels into alphabetical order, (5) identifying double letter errors in a draft leaflet and (6) remembering to press buttons at predefined times during the task. The first five activities were relatively continuous and take a substantial amount of time to complete, while the sixth activity involved remembering to carry out an action at two specified times. Completing all of the activities fully is estimated to take over one hour; however, as participants are given only 15 minutes they must plan and organise their time in order to successfully follow the task instructions. Thus, this task is hypothesised to place demands on various executive abilities, including set shifting, inhibition, initiation, planning, monitoring and prospective memory.

The current research used a modified version of the Hotel task. This task was administered under two conditions. The 'standard' administration condition of the Hotel Task was based on the original Hotel Task described by Manly and colleagues (2002; see Appendix 4 for task instructions). After presenting the task instructions, participants were asked to repeat the primary goal of the task. If participants did not clearly state that they should attempt to complete as much of each of the activities as they could, spending equal amounts of time on each activity, these instructions were repeated. Once the task had begun, no further prompts were given except when participants had attempted only one activity after five minutes had passed. In this case, participants were given a single reminder to try to complete something from each of the different activities.

For the purposes of this study a novel 'structured' condition was created that involved repeating the Hotel Task with additional instructions (Appendix 5). In this condition, participants were presented with a 'recommended plan' which

they were told would assist them in completing the task most efficiently. This listed a recommended order of completion for the activities, allocating three minutes per activity, for example “Compiling Individual Bills 11:00 – 11:03” (Appendix 6), and also included the correct times to ‘open and close the garage doors’. Participants were also told that the researcher would prompt them when it was time to move onto the next activity on the list. Once the task had begun, participants were verbally prompted to move onto the next item on the recommended plan every three minutes (“It is now time to move onto the next task on the list”). This prompt was given five seconds before the clock indicated the three minute period was complete, to allow time to leave task materials one side (e.g. 11:02:95, 11:05:95, etc.). If participants had already switched activities, the prompt was substituted with a reminder of the number of minutes that had passed (e.g. “Six minutes have now passed”). The order of activities was fixed across groups and participants, so that any task order effects were systematic. The order of activities was chosen so that the activities involving sorting materials (coins and labels) were interspersed between activities which involved fewer materials (bills, directory and proofreading).

For both conditions, two main types of outcome measures were collected. The ‘executive’ outcome measures were similar to those described by Manly and colleagues (2002) in that they relate to how well the task instructions were followed. These included the number of activities attempted, the total time spent on each activity, the deviation from the optimal time per activity (180 seconds), and the time at which the buttons were pressed. Additionally, the number of times the clock was checked was recorded. Where participants did not attempt an activity at all, a penalty time deviation of 180 seconds was assigned. If participants did not remember to press the buttons during the task at all, the participant was assigned the value of the largest observed time discrepancy across both groups. In contrast to the original Hotel Task, performance on each of the activities was also recorded. These second set of outcome measures related to the actual performance of participants on each

of the five continuous activities (i.e. number of items completed or correctly sequenced). These scores were standardised by calculating how many items the participant completed on average in 60 seconds ('performance efficiency' scores). Where participants did not attempt the activity at all during the task, the performance efficiency was recorded as zero.

2.4.2 Background Measures

2.4.2.1 Demographic Information and Employment Status

A record form for demographic information and inclusion criteria was used for the study (Appendix 7). This recorded the age, gender and ethnicity of all participants. Participants were asked about the number of years of full time education they had completed, as well as to describe their current employment status. The handedness of each participant was recorded. The approximate date of diagnosis of MS was recorded for the RRMS group, and participants in this group were asked whether they had experienced a relapse in their condition during the past four weeks. All participants were asked the inclusion and exclusion screening questions, as described above.

Details about current and past employment, obtained from a brief interview, were recorded on an Employment Questionnaire (Appendix 8). In particular, participants were asked to state whether they were currently working, and if so, if this was part-time or full-time, paid or unpaid, work. Employed participants were asked to say how many hours work they do during an average week. Unemployed participants were asked when they became unemployed, and whether they considered themselves to hold other roles (such as full time parent or carer). Participants were also asked to provide their current job title, or if unemployed, to describe the highest work position they have held if applicable. This information was coded under the system devised by the Standard Occupational Classification 2010 (*SOC2010*; ONS, 2010; Appendix 9), a comprehensive list of jobs divided into nine categories ranging from elementary occupations to managers, directors and senior

officials. A tenth category was added for those participants who reported they had never held a job.

Additionally, participants in the MS group were asked questions about how MS has impacted on their work or primary role. These questions were based on the information provided by Smith and Arnett (2005) and included a general question about the impact of MS overall, as well as questions about the impact of physical/neurological symptoms, fatigue/tiredness and cognitive impairments on their work. Responses were given on a five point Likert scale (0-4) where higher ratings indicate greater impact.

2.4.2.2 Mobility

The Guy's Neurological Disability Scale – Lower Limb disability scale (GNDS-LL; Sharrack & Hughes, 1999; Appendix 10) is a clinical disability measure based on patient self report, and the Lower Limb subscale is one of 12 functional domains included in the GNDS. Participants are asked about their typical method of mobility indoors and outdoors over the previous month. It allows patients' mobility to be categorised on a six point scale: 0 = Walking is not affected, 1 = Walking is affected but patient is able to walk independently, 2 = Usually uses unilateral support to walk outdoors, but walks independently indoors, 3 = Usually used bilateral support o walk outdoors, or unilateral support to walk indoors, 4 = usually uses wheelchair to travel outdoors, or bilateral support to walk indoors, 5 = usually uses a wheelchair indoors. This questionnaire has been reported to have satisfactory psychometric properties and appears reliable and valid (Sharrack & Hughes, 1999). Of the GNDS subscales, the GNDS-LL has been found to have the highest correlation to the EDSS (r = 0.88; Hoogervorst et al., 2001), which has been used extensively in research on MS but requires a neurological examination of the patient.

2.4.2.3 Intellectual Functioning

The National Adult Reading Test, revised version (NART; Nelson & Willison, 1991) was used to provide an estimate of the participants' premorbid intellectual functioning. This task involves participants pronouncing aloud 50 irregularly spelt words, with the number of errors recorded. Performance on the NART is hypothesised to place minimal demands on current cognitive abilities, and rather depends on pre-morbid ability and prior knowledge of the correct pronunciation. The NART has been shown to have good reliability (e.g. O'Carroll, 1995). In terms of validity, it has been shown to correlate with measures of childhood intelligence (e.g. Crawford, et al., 2001), even in the context of mild neurological changes (Strauss, Sherman & Spreen, 2006).

The Montreal Cognitive Assessment (MOCA; Nasreddine et al., 2005; Appendix 11) was also administered as a brief screening assessment for milder forms of cognitive impairment. This is a 30 point measure which includes brief tasks assessing visuo-spatial, executive, naming, memory, attention and language abilities. It was developed to serve as a more sensitive screen for early signs of dementia compared to conventional measures such as the Mini Mental State Examination (MMSE), and has the advantage of detecting Mild Cognitive Impairment (MCI) with high sensitivity. The authors report good reliability (inter-rater reliability $r = 0.92$, Cronbach $\alpha = 0.83$), and they recommend a clinical cut off score of below 26 points for MCI. Clinically, the authors also recommend that a single point should be added to the total score for participants who report less than 13 years of full time education, although the raw score was used for the purposes of the current study. There has been some preliminary evidence that the MOCA is more sensitive to cognitive impairment in MS than the MMSE, based on the proportion of people scoring below the threshold (Ionescu et al., 2011). These authors reported that 40.7% of their sample of people with MS of varying subtypes scored below the cut-off.

2.4.3 Neuropsychological Assessments

2.4.3.1 Processing Speed

The SDMT is a commonly used measure of processing speed in the visual modality in people with MS. The oral response version is recommended to reduce motor demands due to the possibility of upper extremity weakness or incoordination associated with MS (Benedict et al., 2002). In the SDMT, a series of nine digits, each paired with a unique symbol, is presented at the top of an A4 sized sheet. Included in the nine symbols are three mirror-image pairs. The lower part of the sheet is filled with symbols in a pseudo-randomised order, and participants are requested to say what number goes with each symbol in sequence as quickly as possible. The SDMT has been shown to have respectable inter-rater reliability, with values over 0.80 consistently reported across various periods of time, as well as good validity (Benedict et al., 2008; Drake et al., 2010; Morrow et al., 2010). This measure has been found to be sensitive to the cognitive difficulties associated with RRMS with high effect sizes (Prakash et al., 2008). It has been demonstrated to be the neuropsychological assessment with the strongest association with brain imaging findings in this population (Strauss, Sherman & Spreen, 2006). Compared to the PASAT, another commonly used processing speed measure in MS which has been reported to be frustrating for participants (e.g. Aupperle et al., 2012), the SDMT takes less time to administer, is reported to be less frustrating and has been found to have slightly better predictive validity (Drake et al., 2010).

2.4.3.2 Learning and Memory

The Logical Memory I and II subtests of the Wechsler Memory Scale – Fourth Edition (WMS-IV; Wechsler, 2009) was administered to all participants as a measure of auditory learning/memory. The WMS-IV is a battery to assess various aspects of memory, and the Logical Memory subtests contribute to the Auditory Memory index. The overall WMS-IV has been normed on a U.S. sample of 1,400 people. Participants were read two unrelated short stories which comprised of 25 concepts each. They were asked to recall each story

immediately after hearing it (Immediate Recall) and again 20 to 25 minutes later (Delayed Recall). Participants were encouraged to recall the story as close to the original reading as possible. Reliability coefficients of the Logical Memory I subtest for normative group adults aged between 30 and 64 ranged between 0.81 and 0.86. These values for the Logical Memory II subtest ranged from 0.81 to 0.90. Corrected test-retest reliability for these subtests have been found to be 0.74 and 0.71 (Wechsler, 2009).

2.4.3.3 Working Memory

Working memory was assessed using the Digit Span test included in the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV; Wechsler, 2008). Only the DS-Forward (DSF) and DS-Backwards (DSB) subtests of this task were administered. This involves reading increasingly long strings of numbers to participants, who are required to repeat them back immediately. The DSF subtest involves repeating the numbers in the same sequence as the experimenter, while the DSB subtest involves repeating the numbers in the reverse order. The test is discontinued once the participant incorrectly repeats two number strings of the same length. For the age groups between 30 and 64 years of age, the DSF task has been reported to have internal reliability values ranging from 0.77 to 0.84 and the reliability values for the DSB task has been found to have reliability values of 0.82 to 0.86 for these age ranges (Wechsler, 2008). Corrected test-retest reliability for these subtests have been found to be 0.77 and 0.71 respectively (Wechsler, 2008).

2.4.3.4 Executive Functioning

To ensure that a range of executive abilities theorised to be important in completion of everyday activities are measured, three tests of executive functioning were administered: the Hayling Test, the TMT and the Fluency Test from the D-KEFS.

The Hayling Test is a measure of response initiation and inhibition in two sections. In the first section 15 incomplete sentences are read by the

experimenter and the participant is instructed to provide a word which meaningfully completes the sentence as quickly as possible. Participants typically provide a rapid and stereotyped response (e.g. “Too many men are out of… work”). In the second section participants were required to provide unconnected words to 15 similar incomplete sentences (e.g. “The captain wanted to stay with the sinking… trousers”). The data recorded is the time taken for section 1 (response initiation), the time taken for section 2 and the error score for this section (response suppression and strategy formation) and finally the overall efficiency score. Burgess and Shallice (1997) report that the overall Hayling score has an internal reliability of 0.76.

The TMT is an assessment of divided attention and cognitive flexibility. This task has two conditions. TMT-A provides control data on the lower-level processes which contribute to performance on part B, namely motor speed and sequencing ability. TMT-B has an additional executive component, namely switching between sequencing letters and numbers. As motor impairments are common in people with MS, it is particularly important to consider motor speed when interpreting performance on this task. The time taken to complete the tasks is recorded. Errors are not recorded, as it is assumed that errors are reflected in the fact that these lengthen completion time. The reliability values for Parts A and B have been reported as 0.98 and 0.67 respectively (Lezak, 1995).

The D-KEFS Fluency task assesses the ability to generate words while following certain rules. Participants are asked to carry out two fluency tasks. Letter Fluency involves generating as many works beginning with a specific letter (F, A and S) as possible within one minute. Category Fluency requires generating as many words as possible in one minute from a specific category (‘Animals’ and ‘Boys’ Names’). The Category Switching subtask was not administered. The authors report ‘high’ internal consistency and high test-retest reliability for Letter Fluency ($r = 0.80$), with ‘marginal’ internal

consistency and satisfactory test-retest reliability (r = 0.79) for Category Fluency (Homack, Lee & Riccio, 2005).

2.4.4 Questionnaire Measures

2.4.4.1 Fatigue

The Modified Fatigue Impact Scale (MFIS; Fisk et al., 1994; Appendix 12) from the Multiple Sclerosis Quality of Life Index (MSQLI; Ritvo et al., 1997) is a 21 item multidimensional scale developed to assess the perceived impact of fatigue on daily activities. Responses are given on a five point Likert scale (0 to 4), where higher ratings indicate greater fatigue. The total score is calculated by adding the ratings for each item, with a maximum score of 105. The subscales include: Physical (maximum 45), Cognitive (maximum 50) and Psychosocial (maximum 10) dimensions. The internal consistency of the MFIS-total score has been reported as 0.96, with similar values for the applicable subscales (Amtmann et al., 2012). Marrie and colleagues (2003) also reported an internal consistency reliability value of 0.96, with a test-retest reliability value of 0.87 for cognitively unimpaired people with MS. They did not find any difference in the reliability between people with MS who displayed cognitive impairment and those who did not.

2.4.4.2 Apathy & Executive Functioning

The Apathy Scale from the Frontal Systems Behaviour Scale (FrSBe; Grace et al., 1999) provides a measure of behavioural indices of apathy, and is available in self report and family rated versions. The FrSBE was developed to serve as a brief rating scale which aims to measure behaviours associated with damage to the frontal systems of the brain. The other subscales of questionnaire measure Executive Dysfunction and Disinhibition. The FrSBe has been found to be a sensitive measure of behavioural change in people with MS (Chiaravalloti & DeLuca, 2003). Both the self rating and the family rating forms were administered to the group with MS, while the control group completed the self rating form only. Grace and colleagues (1999) report

internal reliability values in the normative sample of 0.72 for the self-rated Apathy scale, and the corresponding value for the family rating form is 0.78. The Executive Dysfunction subscale ratings were 0.79 (self) and 0.87 (family) and the Total scale ratings were 0.88 (self) and 0.92 (family).

2.4.4.3 Depression

The Centre for Epidemiological Studies of Depression Scale (CES-D; Radloff, 1977; Appendix 13) is a freely available 20 item self report measure of current symptoms of depression which has been validated for use with the general population and used in previous research in MS. Responses are given on a four point Likert scale (0-3) where higher scores indicate greater frequency of occurrence of that item. Four of the 20 items are reverse scored. Responses are summed to a Total score, with a maximum value of 60. The traditional clinical threshold for depression is a score of 16 or above. Radloff (1977) reported internal consistency values ranging from 0.85 to 0.90 across studies. It has been found to have good predictive value in identifying MS patients with depression (Pandya et al., 2005), with 75% of those who scored above 16 points being found to have diagnosable depressive disorders. The CES-D may be particularly appropriate for this population as it is felt to minimize reliance on the physical symptoms of depression which overlap with MS symptoms (Diamond et al., 2008). Measures of the non-somatic symptoms of depression have also been suggested to be more strongly associated with cognitive dysfunction (Sundgren et al., 2013).

2.4.4.4 Instrumental Activities of Daily Living

The Instrumental Activities of Daily Living Scale (IADL; Lawton & Brody, 1969; Pantoni et al., 2005; Appendix 14) is an informant report measure of more complex everyday functional activities which require a broader range of cognitive abilities, in comparison to ADLs which are more simple, physical self maintenance tasks (Monaci & Morris, 2012). This is an informant rated scale consisting of eight daily living abilities, such as using the telephone and managing medications. The wording of the items was modified slightly in

order to allow it to be completed by an informant, rather than being worded as interview questions. Responses are given on a three or four choice scale, ranging from full independence to not displaying the ability at all, with the additional option of recording 'not applicable' if the person carries out the activity less than once a month. Previous research suggests that milder forms of cognitive impairment (e.g. early dementia) are more strongly associated with IADLs rather than ADLs alone (Monaci & Morris, 2012) and a survey of people with MS suggested impairments in IADLs are more common than ADL difficulties (Paltamaa et al., 2006).

2.5 Materials

2.5.1 Hotel Task

This task was recreated based on the published description of Manly and colleagues (2002) with additional information obtained from a colleague of Dr Manly (Fish, personal correspondence). This task includes six separate tasks with associated materials. These are described in turn below. The recommended plan for the structured version of this task was presented on a laminated A4 card (Appendix 6). A brief summary of the instructions for each task was presented to each participant on a laminated A5 sized card (Appendix 15). Tasks were positioned in the same locations for all participants and across both conditions (Figure 2).

2.5.1.1 Compiling Bills

The materials for this task were identical to those used by Manly and colleagues (2002). Participants were presented with a list of 100 associated names, bill items and costs (e.g. Mr Ford – room service – 1.95) which was labelled as a 'till roll' of charges. These charges were presented over five laminated pages. Participants were also given 10 A4 sized pages (5 pages for each version of the task), with one 'client' listed on each page and space to list the bill items and costs (Appendix 16).

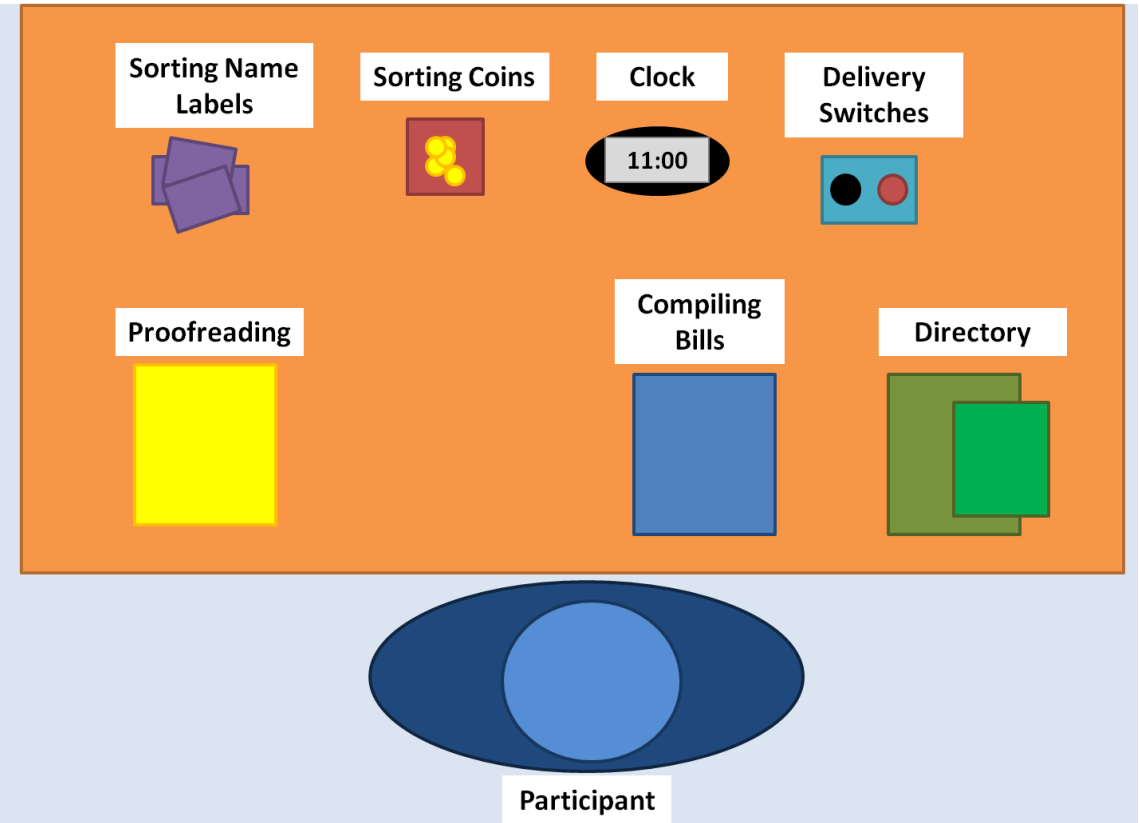


Figure 2: The positioning of task materials at the beginning of the Hotel Task

2.5.1.2 Sorting the Charity Collection

Participants were presented with a small box containing 196 coins; 21 (10.7%) of which were foreign currency (EU Euro, Hungarian Florint, Danish Kronor). The composition of British coins were identical to the coins used by Manly and colleagues, and included 5x1p, 4 x 2p, 96 x 5p, 46 x 10p and 24 x 20p. Participants were also given 20 plastic money bags. The same materials were used for both the standard and structured versions of the task.

2.5.1.3 Looking Up Telephone Numbers

Participants were presented with a small local business directory (thomsonlocal.com, Lambeth 2013 edition) along with a list of 50 companies listed in the directory (25 companies for each version of the task; Appendix 17). As participants were expected to differ in their experience of using paper

directories, the A to Z section at the rear of the directory was removed, so that all participants would have an identical task of searching the “Businesses by Type” listings.

2.5.1.4 Alphabetising Name Labels

A pile of 100 index cards were presented to participants, with a first- and surname printed on each one. A different pile of 100 cards with different names was used for the second version of the task. The names were chosen from lists of the most common and popular names in the United Kingdom. Each surname was unique and not repeated, while first names were used up to two times per pile. After administration of the task, the pile of index cards was shuffled.

2.5.1.5 Proofreading the Hotel Leaflet

The materials for this task were identical to those used by Manly and colleagues (2002; see Appendix 18 for a sample of the stimulus). Nine pages of text were presented to participants and these were labelled as a ‘draft of the hotel leaflet’. The main body of the text was typed in single spaced Arial font, size 11, which was divided into subsections and paragraphs. Both versions of this document contained the same text, but had different spelling mistakes consisting of double letter repetitions (e.g. ‘neww’ instead of ‘new’). The number of spelling mistakes was identical between the two versions (138 total errors), and these were matched so that a similar number of errors were found in each paragraph of text.

2.5.1.6 Opening and Closing the Garage Doors

A white two way push on/off dimmer light switch, mounted on a chrome pattress box, was used to represent the garage door controls. One of the dimmer switches was painted black and one red. A digital clock was provided to participants, which displayed the hour and minute only (HH:MM). This clock was set to 11:00 at the beginning of the task, and was covered with a small,

white cardboard box, which could be quickly lifted and replaced in order to check the clock.

2.6 Procedure

2.6.1 Informed Consent

At the beginning of the research session, participants were given a brief reminder of the research goal and rationale, followed by the opportunity to ask questions about the research and their involvement. Participants were then asked to provide written informed consent to participate, as well having the opportunity to indicate whether they would like to receive a generic summary of the research findings. Participants with RRMS were given the additional option of having a brief summary of their performance on the clinically validated tasks sent to their consultant neurologist (see Appendix 19 for copies of the consent forms).

2.6.2 Research Session

All participants within each group completed the research tasks in an identical order. The background information interview was carried out initially, followed by the neuropsychological tasks. In total, these tasks took approximately 90 minutes, although the session took longer when participants had more questions or provided more information during the interview phase. A break was recommended after completing the first half of the tasks, although only a very small number of participants decided to take a break during the session. Participants with RRMS were given the option of completing the questionnaire measures before, during or after the research session, as was most convenient. Healthy control participants all completed the questionnaires at the end of the research session.

2.6.2.1 Interview

Participants were next asked questions about their demographic characteristics, and the list of inclusion and exclusion criteria screening questions were asked if these had not been asked at the point of first contact. Participants with RRMS were administered the GDNS-LL.

All participants were asked about their employment using the Employment Questionnaire, and participants with RRMS were asked to rate the impact of symptoms clusters on their work or primary role.

2.6.2.2 Neuropsychological Assessment Tasks

The order in which the neuropsychological tasks were completed was identical for all participants (Table 1). The SDMT was administered initially, followed by the Letter Fluency and Category Fluency subtests of the D-KEFS Fluency test. The Hotel Task was then introduced, and the Standard Condition was administered. Next, the MoCA was administered, although the fluency component of this task was skipped as this had been completed during the earlier Fluency test. Participants were informed that they had completed half of the tasks, and were offered a break.

Table 1: Order of administration of the research tasks.

First Half	**Second Half**
Informed Consent	Logical Memory I
Screening Questions (& GDNS-LL)	Hotel Task – Structured Condition
Employment Questions (& Impact Scale)	Logical Memory II
SDMT	Digit Span
Verbal Fluency	Hayling Test
Hotel Task – Standard Condition	Trail Making Test Parts A & B
MoCA	NART - R

GNDS-LL: Guys Neurological Disability Scale – Lower Limb disability; SDMT: Symbol Digit Modalities Test; MoCA: Montreal Cognitive Assessment; NART-R: National Adult Reading Test – Revised.

Logical Memory I was administered next, followed by the Structured Condition of the Hotel Task. As this task takes 15 minutes, in addition to time to arrange

the materials and review the instructions, sufficient time had generally passed in order to administer the delayed recall memory task (Logical Memory II). The Digit Span, Hayling Test and TMT Parts A & B were next administered in that sequence. As the final task, participants completed the NART-R.

2.6.2.3 Questionnaire Measures

Participants with MS varied in terms of when they completed the self reported questionnaires. Participants could choose to complete these at one of three times in order to accommodate participants who were experiencing fatigue: (1) Prior to the research session (n = 8). This was typically the case when participants were given the Participant Information Sheet in person, and completed the research session at least one week later. (2) On the day of the research session (n = 8). This was typically the case for participants who had not completed the questionnaires in advance and agreed to complete the questionnaires at the end of the research session. (3) After the research session (n = 3). This was typically the case for participants who reported fatigue at the end of the research session, or had to leave promptly due to other commitments. In this case, participants were given a stamped addressed envelope and returned the questionnaires by post.

Similarly, informants varied by when they completed the two informant rating questionnaires. Again these were completed before (n = 8), on the day of (n = 3), or after (n = 8) the research session.

All participants in the control group completed the three self-report questionnaires at the end of the research session.

2.6.3 Payment

Participants in both groups were paid £10 for completing the research session and completing the self-report questionnaires. Informants (MS group only) were paid £5 for completing the two informant rating questionnaires.

2.6.4 Research Summaries

During the informed consenting process, participants could opt to receive a summary of the overall research findings. Participants also had the option to have a brief summary of their individual performance on the previously validated neuropsychological and questionnaire measures sent to their consultant neurologist.

3 Results

3.1 Overview of Results

This chapter will describe the results of the statistical analyses chosen to test the predictions of the hypotheses. Initially, the results of the background neuropsychological and questionnaire data will be presented. Next the results from the analyses of the Hotel Task data will be described in order of the hypotheses presented in the introduction, and where appropriate the results of the Hotel Task variables will be compared to the results from the background assessments.

The outcome measures from the Hotel Task can be categorised into two broad groups:

(1) Hotel Task executive functioning variables for both conditions. These include measures of the degree to which task rules were followed (e.g. number of activities attempted, deviation from the optimal time per activity of 180 seconds), time monitoring (number of clock checks) and prospective memory (deviation from the expected button press times).

(2) Hotel Task performance efficiency variables for each of the attempted tasks for both conditions. These data are summarised as the number of items correctly completed within one minute on each of the five ongoing activities.

The main dependent variables from the traditional neuropsychological tasks and questionnaires were the raw scores as described in the task manuals. If appropriate, subscale scores were also calculated.

3.2 Sampling Distributions

Where possible, data were analysed using parametric analyses, as it has been suggested that parametric assessments have greater power to reject a

false null hypothesis compared to parametric tests (e.g. Howell, 2012). Prior to testing the hypotheses, the data were analysed to establish whether these were drawn from a normally distributed population. Initially, the data were visually presented in box plots and checked for symmetrical distribution. Data was checked for outliers. Where these were found to be valid responses within the task, they were not removed as they likely represent impaired performance. As some of the variables appeared to be skewed, the assumption of normal distribution was checked statistically using the Shapiro-Wilk test. The data from these analyses is presented in Appendix 20. Where the sample distribution was found to significantly differ from the normally distributed population, the data were transformed with the aim of achieving a normal distribution. This was done using Tukey's 'ladder of powers' (see Erikson & Nosanchuk, 1992). In effect, this involved transforming the data using a transformation appropriate to the type and magnitude of skew, and rechecking the sampling distribution. Where the transformed data set did not meet the assumption of normal distribution, non-parametric tests were used.

3.3 Level of Significance and Standardised Data

In order to minimise the likelihood of Type I errors, that is rejecting the null hypothesis incorrectly, the criteria for significance was adjusted for secondary analyses. For analyses relating to the main dependent variables, including the Hotel Task variables and the primary background neuropsychology and questionnaire variables, alpha level was set at 5%. For all other analyses, only those statistics significant at the 1% level are discussed.

Furthermore, where possible, group difference data were calculated and displayed using *z* scores, which state the number of standard deviations above or below the control group mean, and effect sizes, which display the size of the difference between groups on a standardised scale. The effect sizes are calculated as Cohen's d (Cohen, 1988), with the following guidelines for interpretation: "small", $d = 0.2$, "medium" $d = 0.5$ and "large" $d = 0.8$.

3.4 Demographic Information

The RRMS and healthy control groups consisted of 19 individuals each. The demographic characteristics of the groups are summarised in Table 2. The RRMS and healthy control (CT) groups were matched for age and gender at a group level, and attempts were also made to match groups on years of full time education. The groups did not differ in terms of age; $t(36)= 1.31$; $p = .200$, years in full time education; $U = 230.00$; $p = .154$, or estimated FSIQ; $t(36) = -1.67$, $p = .104$. Groups did significantly differ in terms of MOCA total score with RRMS participants obtaining a lower score than control participants; $t(36) = -2.459$, $p = .104$. There was no significant difference between groups in terms of gender; $\chi^2 (1) = .146$, $p = 1.000$, handedness; $\chi^2 (1) = .146$; $p = 1.000$, ethnicity; $\chi^2 (1) = .000$; $p = 1.000$, or current employment status; $\chi^2 (1) = .106$; $p = .744$. Considering the participants who were employed at the time of the assessment only, no group differences were observed in working hours; $t(17) = .211$, $p = .889$.

Table 2: Demographic characteristics of participants by group

Dependent Variable		Mean (SD) / Median (IQR) / Ratio		Statistic	*p*
		RRMS	Control		
Gender	F:M[+]	14 : 5	15 : 4	$\chi^2 (1) = .146$	1.000
Age (years)		46.05 (9.82)	42.26 (7.99)	t (36) = 1.305	.200
Education (years)		12 (11 – 14)	15 (12 – 16)	U = 230.00	.154
NART-R	Estimated FSIQ^	103.15	108.79	t (36) = -1.669	.104
MOCA	Total Score	25.84 (2.09)	27.26 (1.41)	t (36) = -2.459	.019
Handedness	Right : Left	18 : 1	18 : 1	$\chi^2 (1) = .362$	1.000
Ethnicity	White : Other	18 : 1	17 : 2	$\chi^2 (1) = .000$	1.000
Employment	W:NW*	9 : 10	8 : 11	$\chi^2 (1) = .106$	.744
	Hours p/w	40.61 (12.87)	39.55 (8.94)	t (17) = .211	.889

[+]Female to Male ratio *Working to Not Working ratio
^Summary data back transformed

3.5 Clinical Characteristics

3.5.1 Disease Duration

Participants in the RRMS group reported that they received a diagnosis of MS on average 10.61 years prior to the assessment (SD = 7.21), and this figure ranged from 2.5 years to 28.0 years since diagnosis.

3.5.2 Physical Disability and Fatigue

Figure 3 displays data on physical disability, indexed by count data on the number of participants with RRMS who received each rating on the GNDS-LL, with rating 1 ("Walking is affected but patient is able to walk independently") as the modal value.

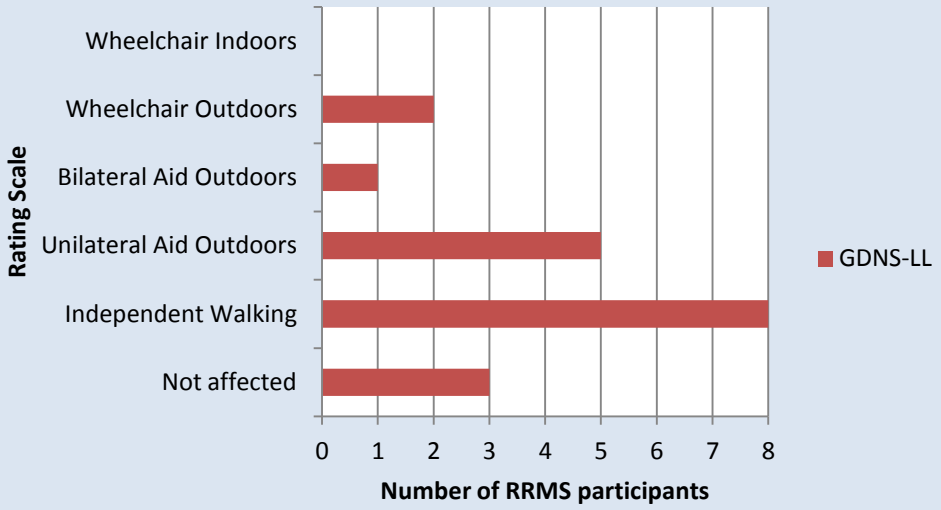


Figure 3: Frequency count of the number of RRMS participants receiving each rating on the Guys Neurological Disability Scale, Lower Limb subscale (GNDS-LL); a measure of mobility.

In terms of fatigue (Table 3), participants with RRMS reported significantly greater levels of overall fatigue than healthy controls; $t(35) = 4.636$, $p < .001$. In terms of the MFIS subscales, participants with RRMS were found to have significantly higher scores on each scale compared to healthy control participants using the 1% significance criterion: Physical scale; $t(35) = 5.308$,

p <.001, Cognitive scale; *U* = 78.00, *p* = .004, and Psychosocial scale; *U* = 75.00, *p* = .003.

Table 3: Self ratings of fatigue as index by the Modified Fatigue Impact Scale

Dependent Variable		Mean (SD) / Median (IQR)		*z* score	*p*	Effect Size (*d*)
		RRMS	Control	RRMS		
MFIS	Total	47.28 (21.53)	20.26 (13.14)	+2.06	<.001	1.504
	Physical	22.61 (9.94)	8.16 (6.32)	+2.29	<.001	1.722
	Cognitive	21 (12-30)	13 (4-17)	+1.48	.004	1.034
	Psychosocial	4 (2-7)	2 (1-3)	+1.75	.003	1.090

3.5.3 Mood

Participants with RRMS reported a significantly higher level of depression symptoms than healthy controls; *t*(35) = 2.65, *p* = .012, *d* = .859 (Table 3). Eleven of 18 participants (61%) obtained a CES-D score equal to or greater than 16 points (the recommended clinical cut off for the general population). Seven participants (39%) had a total CES-D score of 21 or higher (the recommended clinical threshold for primary care health settings). Three of 19 healthy control participants (16%) obtained scores above 16 on the CES-D.

Table 4: Depression self ratings as indexed by the Centre for Epidemiological Studies: Depression (CES-D) scale

Dependent Variable		Mean (SD)		*z* score	*p*	Effect Size (*d*)
		RRMS	Control	RRMS		
CES-D	Total Score^	20.02 (3.45)	9.71 (1.47)	+1.42	.012	.859

^Summary data back transformed.

3.5.4 Apathy and Behaviour Change

Data on the FrSBe total score and subscales are presented in Table 5 and Table 6. Participants with RRMS reported significantly higher current levels of apathy compared to healthy control participants as measured by the FrSBe; *t*(20) = 3.158, *p* = .005, and the self reported apathy of the RRMS group did not differ from the informant ratings; *t*(16) = 1.758, *p* = .098.

In terms of behaviour associated with frontal lobe abnormalities overall, participants with RRMS reported greater current behavioural disturbance than healthy controls; $t(24) = 3.481$, $p = .002$ and again this rating did not differ from that of informants; $t(16) = 1.820$, $p = .087$. A similar pattern of results was found for the Executive Dysfunction and Disinhibition subscales of the FrSBe.

Table 5: Current self ratings of people with RRMS compared to healthy controls, as measured by the Frontal Syndrome Behaviour (FrSBe) scale

Dependent Variable		Raw Mean (SD)		*z* score	*p*	Effect Size (*d*)
		RRMS	Control	RRMS		
FrSBe (Currently)	Total	111.22 (33.04)	81.53 (15.20)	+2.14	.002	1.129
	Apathy	36.39 (14.02)	25.47 (4.43)	+2.47	.005	1.025
	Disinhibition	32.72 (8.30)	25.32 (4.42)	+2.14	.002	1.092
	Executive Dysfunction	42.44 (12.96)	30.74 (8.79)	+2.47	.005	1.049

Table 6: Ratings of the behaviour of people with RRMS, currently and prior to MS onset, as measured by the Self Rating and Family Rating versions of the Frontal Syndrome Behaviour (FrSBe) scale

Dependent Variable		Raw Mean (SD)		*z* score	*p*	Effect Size (*d*)
		RRMS	Informant	RRMS		
FrSBe (Currently)	Total Score	110.24 (33.78)	102.65 (32.68)	+.23	.087	.228
	Apathy	36.41 (14.45)	33.12 (13.42)	+.25	.098	.234
	Disinhibition	32.35 (8.40)	27.65 (12.07)	+.39	.063	.433
	Executive Dysfunction	41.82 (13.08)	40.53 (11.30)	+.11	.487	.104
FrSBe (Before MS onset)	Total Score	76.94 (13.17)	77.75 (17.28)	-.05	.872	-.053
	Apathy	21.81 (5.23)	22.69 (7.21)	-.12	.671	-.138
	Disinhibition	25.81 (4.28)	23.81 (4.82)	.42	.173	.439
	Executive Dysfunction	29.69 (4.64)	31.25 (7.31)	-.21	.462	-.071

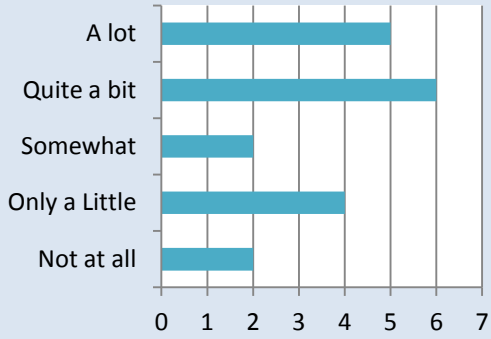
Note: *z* scores calculated based on the mean and standard deviation of the informant ratings for these dependent variables.

3.5.5 Social Impact

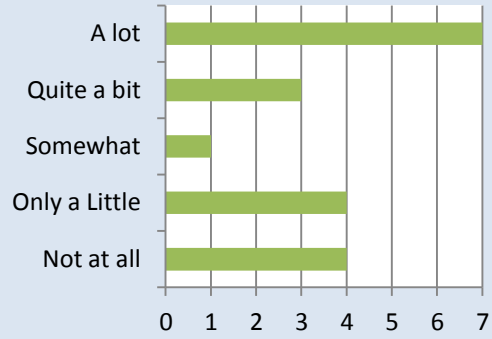
Informant ratings of instrumental ADLs for the RRMS group were available for 16 participants. The median rating was ten, indicating mild difficulty in two

areas or moderate difficulty in one area, with an interquartile range between eight and 15 (the minimum and maximum ratings, respectively).

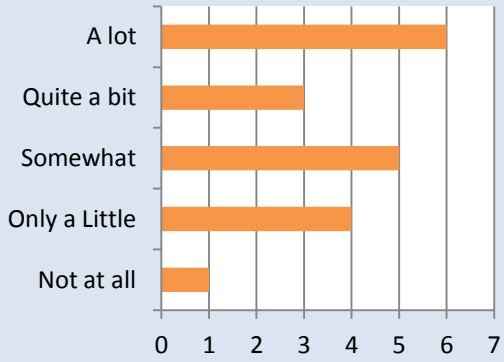
Participants' self ratings of the total impact of MS and associated symptom clusters on their work or main roles are displayed in Figure 4.



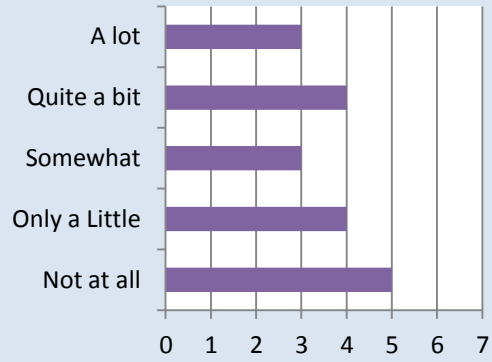
A: Total impact of MS on work or other roles



B: Impact of Physical Symptoms of MS on work/roles



C: Impact of Fatigue on work/roles



D: Impact of Cognitive Symptoms of MS on work/roles

Figure 4: Self reported impact of MS symptoms on work or other primary role, presented as the frequency count of participants endorsing each rating.

3.6 Cognitive Profiles

All participants completed the battery of background neuropsychological assessments (Table 7). The cognitive profile of the group with RRMS is presented in terms of the effect sizes of the difference between the RRMS

and healthy control group (Figure 5) and in terms of the *z* score profile of participants with RRMS as compared to the healthy control group mean and standard deviation is presented (Figure 6). These results will be considered in turn.

3.6.1 Memory and Learning

Participants with RRMS did not significantly differ from healthy controls in terms of immediate memory (Logical Memory I); $t(36) = -.3.750$, $p = .096$. There was a significant group difference for delayed recall memory (Logical Memory II); $t(29) = -2.535$, $p = .017$, with the RRMS recalling less of the stories than the control group. The effect size for this difference was in the large range ($d = -.823$). No difference was found between the groups overall in the amount of information retained across the two points, as indexed by percentage recall; $t(36) = -1.852$, $p = .072$. Considering the two stories that make up this subscale, participants with RRMS were significantly poorer on recall of Story A in both conditions (LM I: $t(31) = -3.427$, $p = .002$, LM II: $t(28) = -3.376$, $p = .002$) with both of these subscale differences significant at conservative alpha level of .01. The groups performed similar to each other on Story B across both immediate and delayed recall.

Table 7: Background neuropsychological task performance

Dependent Variable		Mean (SD) / Median (IQR)		*z* score	*p*	Effect Size (*d*)
		RRMS	Control	RRMS		
Logical Memory	LM I Total	23.42 (6.39)	26.63 (5.11)	-.63	.096	-.555
	LM II Total	19.53 (7.23)	24.42 (4.31)	-1.14	.017	-.823
	LM % Recall	83.15 (14.22)	90.53 (9.99)	-.74	.072	-.601
SDMT	Total Score	50.93 (9.47)	63.03 (9.97)	-1.21	<.001	-1.244
Digit Span	Total^	16.98 (1.26)	19.05 (1.26)	-.47	.114	-.525
Verbal Fluency	Letter	33.05 (8.15)	46.52 (13.38)	-1.01	.001	-1.217
	Category	43.00 (6.94)	47.05 (8.58)	-.47	.118	-.519
TMT	TMT B-A	49.42 (24.93)	31.52 (19.66)	+.91	.019	.797
Hayling Test	Section 1	6 (4-12)	4 (2-7)	+2.05	.034	.735
	Section 2 ^	28.09	19.54	+.89	.189	.434
	S2 Errors	2 (0-8)	0 (0-1)	+2.75	.037	.817

^ Summary data back transformed.

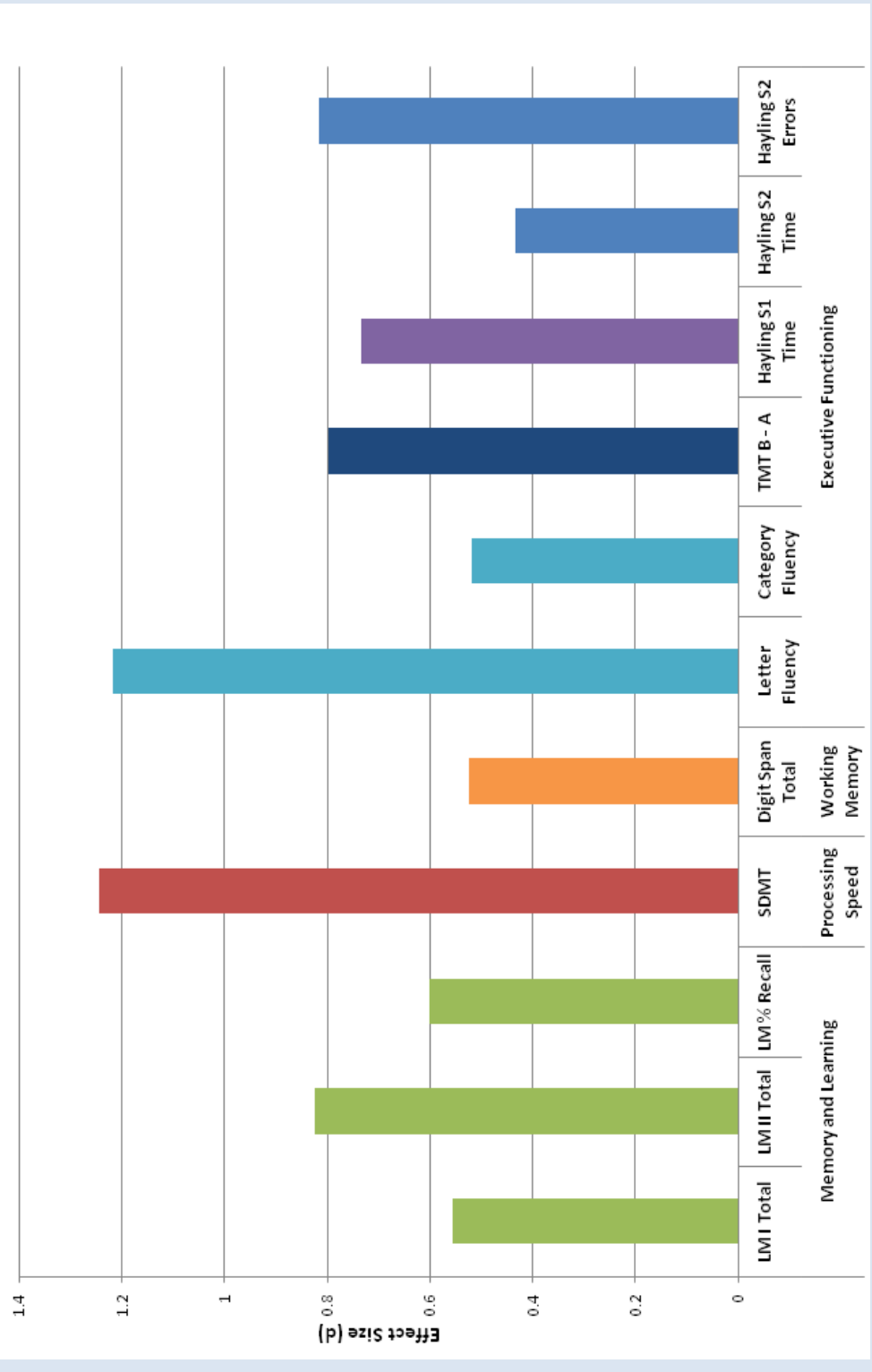


Figure 5: Effect sizes of the between group differences on the traditional neuropsychological tasks.

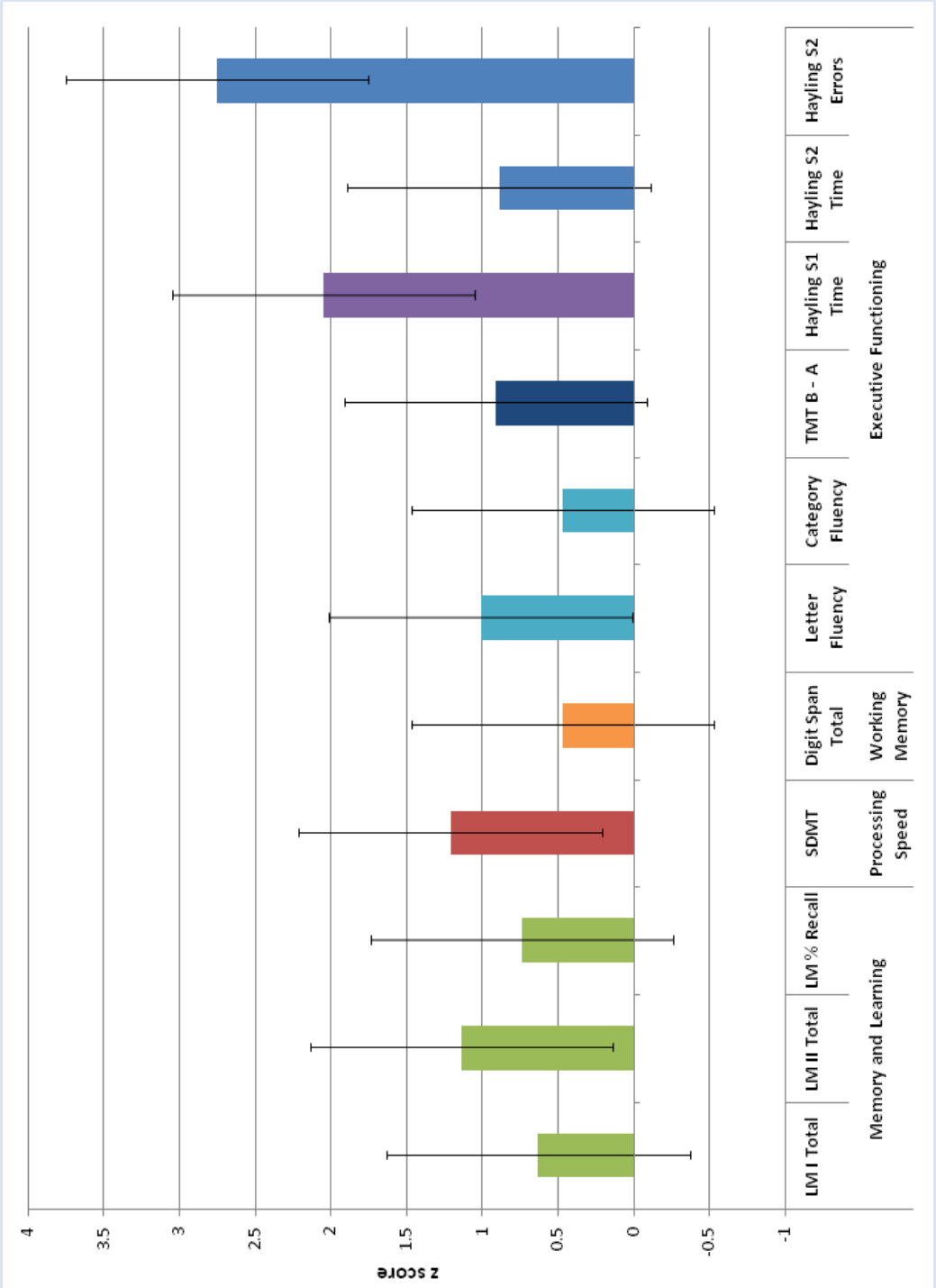


Figure 6: z scores (one SD represented by error bar) for the RRMS group on the neuropsychological tasks.

3.6.2 Information Processing Speed

There was a significant group difference on SDMT total score; $t(36) = -3.833$, $p = <.001$, with the RRMS completing fewer items in 90 seconds compared to healthy controls. The effect size for this difference lay in the large range ($d = -1.244$).

3.6.3 Working Memory

No significant differences were found between the two groups in terms of Digit Span total score; $t(36) = -1.619$, $p = .114$, or either subscale score: DS Forward $t(36) = -1.640$, $p = .110$; DS Backward $t(36) = -1.115$, $p = .272$.

3.6.4 Executive Functioning

3.6.4.1 Verbal Fluency

Participants with RRMS generated significantly fewer words in the letter fluency task compared to healthy controls; $t(30) = 3.750$, $p = .001$, with a large effect size ($d = -1.217$). In contrast, no difference was found between groups on the category fluency task; $t(36) = -1.601$, $p = .118$.

3.6.4.2 Trail Making Task

In order to control for motor response speed, the difference between the completion time on Part A (low demand, sequencing task) and Part B (higher demand, switching and sequence task) was calculated (TMT B – A). Participants with RRMS had significantly longer time differences on this variable, possibly indicating a specific difficulty with the switching component of the task; $t(36) = 2.457$, $p = .019$. The effect size for this difference fell in the medium/large range ($d = .797$).

3.6.4.3 Hayling Sentence Completion Task

The raw data from the Hayling test were analysed. On Section 1 (initiation) participants with RRMS took significantly longer to respond than healthy controls; $U = 108.00$, $p = .034$, with the effect size in the medium range ($d =$

.735). On Section 2 (inhibition), the RRMS group did not significantly differ in terms of response time; $t(36) = 1.338$, $p = .189$, although they did display a significantly greater number of errors than control participants; $U = 109$, $p = .037$, $d = .817$ (large).

3.6.5 Summary of Cognitive Profile

In summary, the largest effect sizes for the group differences were on the SDMT and the Verbal Fluency tasks ($d > 1.20$). Other group differences had equivalent but lower effect sizes ($7.0 < d > 8.5$), including differences on Logical Memory II, TMT B – A, Hayling Section 1 Time and Hayling Section 2 errors (Figure 5). Looking at the *z* score cognitive profile, it can be seen that people with RRMS showed consistently poor performance on tasks such as the SDMT, LM II and Letter Fluency. In addition, participants with RRMS appear to be most impaired on measures from the Hayling Task, with greater deviation from the average performance of the healthy control group (Figure 6).

3.7 Hotel Task

The primary hypotheses of the current study relate to performance on the Hotel Task. These hypotheses will be considered in turn below.

3.7.1 Hypothesis 1

This hypothesis stated that participants with RRMS will perform poorly on the high demand (standard) condition of the Hotel Task relative to healthy controls, in terms of the measures of time discrepancy, prospective memory and clock monitoring. The results of the relevant analyses are presented in Table 8.

The groups did not significantly differ on the number of activities they attempted within the 15 minutes; $U = 213.5$, $p = .339$. The groups did not

differ significantly in terms of time discrepancies across the five activities (as indexed by the overall *z* score); *t*(36) = 1.944, *p* =.060, nor did they significantly differ in terms of time discrepancy on any of the component activities: (1) Compiling Bills; *U* = 116.5, *p* = .061, (2) Directory Search; *t*(36) = 1.531, *p* = .135, (3) Sorting Coins; *U* = 135.5, *p* = .191, (4) Sorting Labels; *t*(36) = 1.143, *p* = .261, (5) Proofreading the Hotel Leaflet; *t*(36)= -1.150, *p* = .258.

Table 8: Performance on the executive functioning variables of the Hotel Task Standard condition.

Dependent Variable		Mean (SD) / Median (IQR)		*z* score	*p*	Effect Size (*d*)
		RRMS	Control	RRMS		
Tasks Attempted	Number of tasks started	5.00 (2.00)	5.00 (1.00)	-.52	.339	-.362
Unsigned Time Discrepancy (seconds)	Total Score (z)	.89 (1.73)	.00 (1.00)	+.89	.060	.631
	Bills	107 (70–180)	65 (35–113)	+.25	.061	.641
	Directory ^	113.85	71.06	+.25	.135	.497
	Coins	129 (35 – 180)	85 (39–107)	+.35	.191	.438
	Labels^	121.22	87.61	+.40	.261	.371
	Proofreading^	61.66	93.32	-.25	.258	-.373
Monitoring	Clock checks^	5.71	10.50	-.73	.014	-.839
Prospective Memory	Open Door	15 (5.5-25.5)	10 (1-30)	-.54	.635	-.157
	Close Door^	32.34	11.75	+.75	.020	-.786

^ Summary data back transformed.

There was a significant difference between groups in terms of clock checks, with the RRMS group monitoring the time less frequently than the healthy control group; *t*(36) = -2.587, *p* = .014. This difference had an effect size in the large range (*d* = -.839). In terms of prospective memory, there was a significant group difference in terms of the time discrepancy for closing the garage doors (pressing the red button) with the RRMS showing a greater discrepancy from the optimal time; *t*(36) = -2.424, *p* = .020, *d* = -.786 (medium effect size). Six people with RRMS completely forgot to press the button to 'close the garage door', while no healthy control participants did this. In contrast, the difference between groups in terms of opening the garage door (pressing the black button) did not reach significance; *U* = 137.5, *p* = .635.

Three participants in the RRMS group forgot to press the button to 'open the doors', while no healthy controls forgot to do this.

3.7.2 Hypothesis 2

The second hypothesis related to performance of participants on the low executive demand, structured condition, with the prediction that participants with RRMS will show a greater improvement than healthy control participants. Statistical analyses were minimised when considering these data in part to reduce Type I error, as participants were effectively told how to manage their time, when to switch tasks and press the buttons, without the need to monitor time independently.

As the overall time discrepancy *z* scores were found to be normally distributed across conditions and groups, a 2 (Group) x 2 (Condition) ANOVA was carried out on these variables. This aimed to assess whether there was an interaction between the group and condition, in terms of discrepancy from the optimal times (Table 9). The interaction was not significant; $F(1, 36) = .061$, $p = .806$ (Figure 7). Looking at the main effects, the main effect for condition was non-significant; $F(1, 36) = .062$, $p = .805$, while the main effect for group was significant; $F(1, 36) = 5.719$, $p = .022$. For both conditions, the RRMS group were less able to keep to the optimal time per activity compared to healthy control participants.

Table 9: Overall time discrepancy (*z* score) means and standard deviations across group and condition for the Hotel Task.

Condition	**Group**		***Condition Total***
	RRMS	**Control**	
Standard	.89 (1.73)	0.00 (1.00)	*.45 (1.47)*
Structured	1.14 (3.35)	0.00 (1.00)	*.57 (2.51)*
Group Total	*1.02*	*0.00*	*.51*

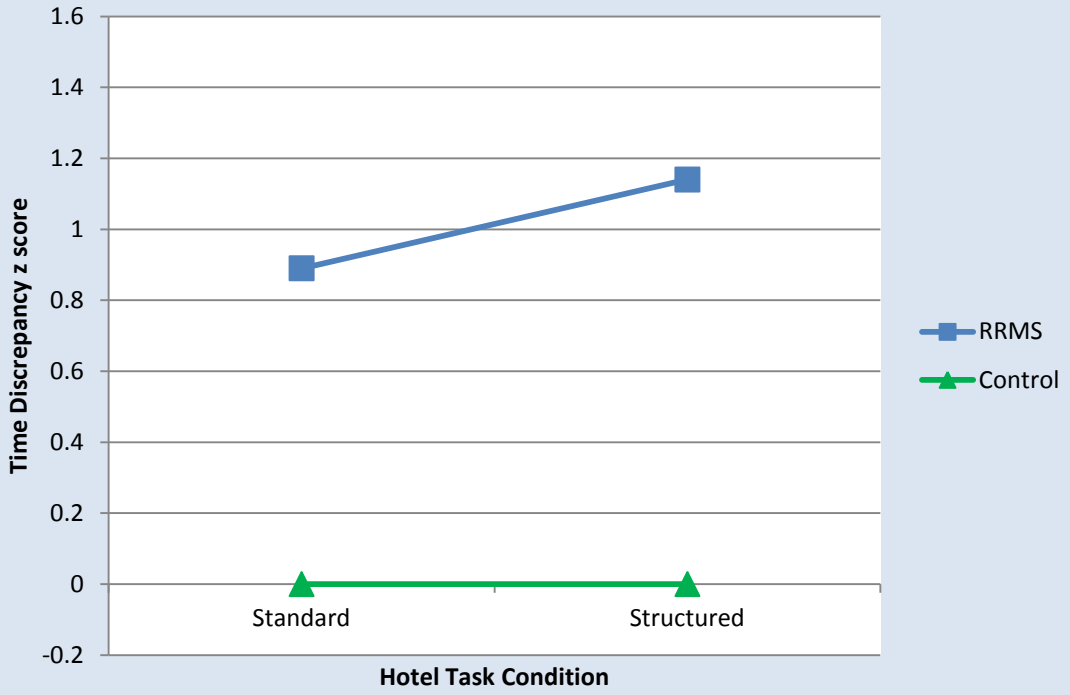


Figure 7: Plot of the mean overall time discrepancy (*z* score) data for the Hotel Task across groups and conditions.

Table 10: Descriptive statistics on performance on the executive functioning variables of the Hotel Task Structured condition.

Dependent Variable		Mean (SD)		*z* score
		RRMS	Control	RRMS
Tasks Attempted	Number of tasks started	5.00 (.00)	5.00 (.00)	.00
Unsigned Time Discrepancy (seconds)	Total Score (*z*)	1.45 (3.35)	.00 (1.00)	+1.45
	Bills	13.32 (20.16)	5.58 (9.05)	-.03
	Directory	28.00 (62.59)	10.32 (11.35)	+1.66
	Coins	15.89 (29.84)	11.63 (13.69)	-.17
	Labels	20.47 (35.76)	14.41 (17.34)	-.51
	Proofreading	21.58 (26.65)	14.26 (17.61)	-.38
Monitoring	Clock checks	1.74 (2.77)	1.68 (2.47)	+.02
Prospective Memory	Open Door	17.47 (14.36)	7.21 (10.11)	+1.05
	Close Door	22.58 (37.05)	4.32 (6.39)	+.39

Descriptive data on the performance of the two groups is displayed in Table 10, which indicates that both groups typically had less deviation from the recommended times in this condition, as expected. All participants attempted

all five tasks. However, comparing the *z* score on the Standard and Structured versions of the Hotel Task, it can be seen that the RRMS group showed greater impairments on the Structured version. This may relate to continued heterogeneity in the performance of people with RRMS, with increased homogeneity of performance in healthy control participants. In support of this, the standard deviations of the RRMS group are more than twice that of control participants for four of the five activities.

3.7.3 Hypothesis 3

Hypothesis three predicted that the performance efficiency of people with RRMS would be lower than that of healthy control participants across both conditions.

The overall *z* score data was found to come from a normally distributed population, and so this was entered into the 2 (Group) x 2 (Condition) ANOVA mixed model design (Table 11). The interaction between group and condition was found to be non-significant, $F(1, 36) = .037$, $p = .849$. Looking to the main effects, the effect of condition was again found to be non significant, $F(1, 36) = .034$, $p = .849$; while the effect of group was significant, $F(1, 36) = 21.971$, $p < .001$. The performance efficiency of the RRMS group was lower for both the Standard and Structured conditions of the Hotel Task (Figure 8). One disadvantage of using *z* score data for this analysis is that it provides no information on how much the performance of control participants differed between conditions. Nonetheless, it is useful in ascertaining whether an interaction is present, as well as comparing across groups.

Table 11: Performance efficiency *z* score means and standard deviations across group and condition for the Hotel Task.

Condition	**Group**		***Condition Total***
	RRMS	**Control**	
Standard	-1.38 (.89)	0.00 (1.00)	*-.69 (1.16)*
Structured	-1.43 (1.12)	0.00 (1.00)	*-.71 (1.27)*
Group Total	*-1.40*	*0.00*	*-.70*

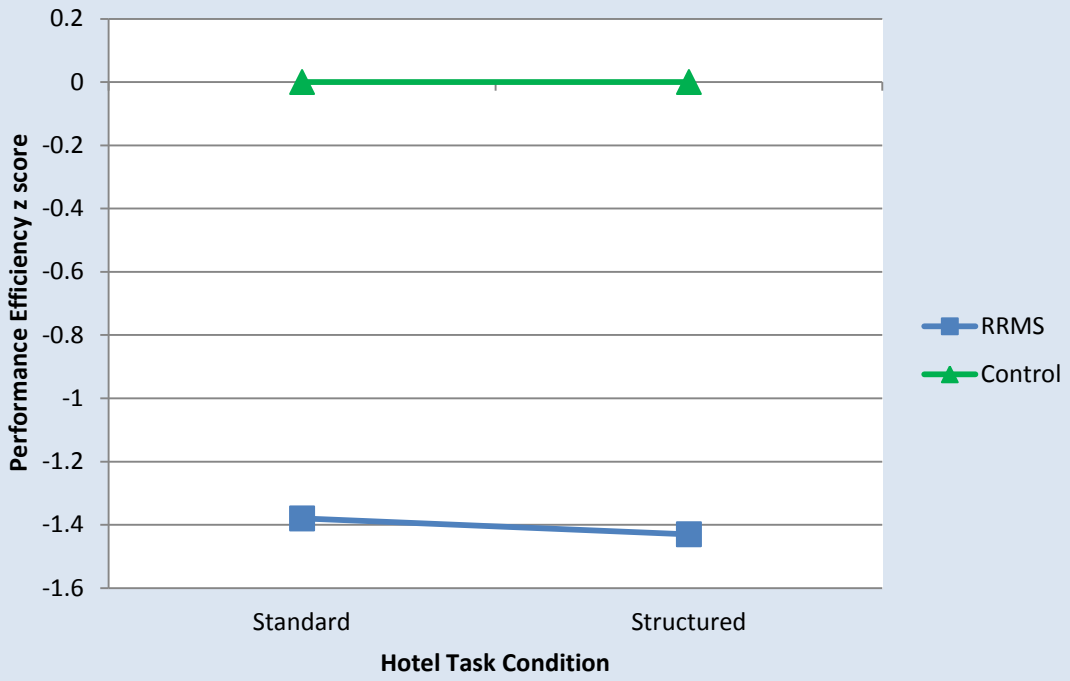


Figure 8: Plot of the mean overall performance efficiency (*z* score) data for the Hotel Task across groups and conditions.

Performance efficiency values for the individual activities of both Hotel Task conditions were typically found to not come from a normally distributed population (see Appendix 21). As such, it was inappropriate to use parametric ANOVA analyses. Instead, the within group differences between conditions were calculated (Table 12), and a Mann Whitney U analysis was used to compare these differences as a non-parametric equivalent to assessing whether a significant interaction is present. These analyses indicated that there was no difference in the pattern of performance efficiency across conditions or groups for: (1) Compiling Bills; $U = 131.0$, $p = .154$, (2) Directory Search; $U = 124.5$, $p = .103$, (3) Sorting Coins; $U = 177.0$, $p = .931$, (4) Sorting Labels; $U = 204.0$, $p = .506$, (5) Proofreading the Hotel Leaflet; $U = 120.0$, $p = .080$.

Table 12: Performance Efficiency Difference scores between conditions on the Hotel Task for the RRMS and healthy control groups

Dependent Variable	Median (IQR)		*z* score	*p*	Effect Size (*d*)
	RRMS	Control	RRMS		
Bills	1.02 (.51 - 2.31)	.54 (.03 - 1.83)	.34	.154	-.482
Directory	.00 (-.30 - .00)	-.23 (-.48 - .00)	.58	.103	-.556
Coins	.48 (-.06 – 1.13)	.44 (.09 – 1.00)	-.07	.931	-.033
Labels	.99 (-.11 – 4.87)	1.56 (-.20 – 4.95)	-.15	.506	.224
Proofreading	.13 (-1.62 – 1.36)	-1.18 (-1.02 – -3.19)	.53	.080	-.598

In order to investigate whether there were between group differences in performance efficiency scores, these were compared using the Mann Whitney U test for both the Standard and Structured versions of the Hotel Task (Table 13). Due to the large number of comparisons conducted, only those results significant at the 1% level are discussed. The activities which best differentiated the RRMS and healthy control groups for both conditions were the Compiling Bills and Proofreading tasks. For the Standard condition, participants with RRMS were less efficient on the Compiling Bills task, U = 302.0, p < .001, d = 1.417 (large effect size) and the Proofreading task, U = 315.0, p < .001, d = 1.653 (large effect size). A similar pattern was observed for the Structured condition: participants with RRMS were less efficient on the Compiling Bills task, U = 288.5.0, p = .001, d = 1.191 (large effect size) and the Proofreading task, U = 300.0, p < .001, d = 1.373 (large effect size).

Table 13: Performance Efficiency scores for both groups on the Standard (HTA) and Structured (HTB) conditions of the Hotel Task

Dependent Variable		Median (IQR)		*z* score	*p*	Effect Size (*d*)
		RRMS	Control	RRMS		
HTA	Bills	1.91 (1.69 – 3.37)	4.04 (3.03 – 6.06)	-1.02	<.001	1.417
	Directory	.00 (.00 - .37)	.50 (.00 - .70)	-.75	.018	.856
	Coins	1.50 (.00 – 2.23)	1.96 (.82 – 2.46)	-.40	.271	.373
	Labels	4.91 (3.08 – 7.01)	8.89 (3.53 – 9.76)	-.01	.034	.733
	Proofreading	3.36 (1.53 – 5.42)	7.45 (4.71 – 9.56)	-1.50	<.001	1.653
HTB	Bills	3.75 (2.97 – 4.86)	5.56 (4.22 – 6.33)	-1.00	.001	1.191
	Directory	.00 (.00 - .13)	.00 (.00 - .36)	-.35	.297	.408
	Coins	1.94 (1.02 – 2.39)	2.32 (1.90 – 2.81)	-.76	.053	.664
	Labels	6.85 (5.05 – 9.79)	9.56 (7.25 – 11.23)	-.82	.011	.898
	Proofreading	3.25 (2.21 – 4.59)	6.07 (4.83 – 8.00)	-1.20	<.001	1.373

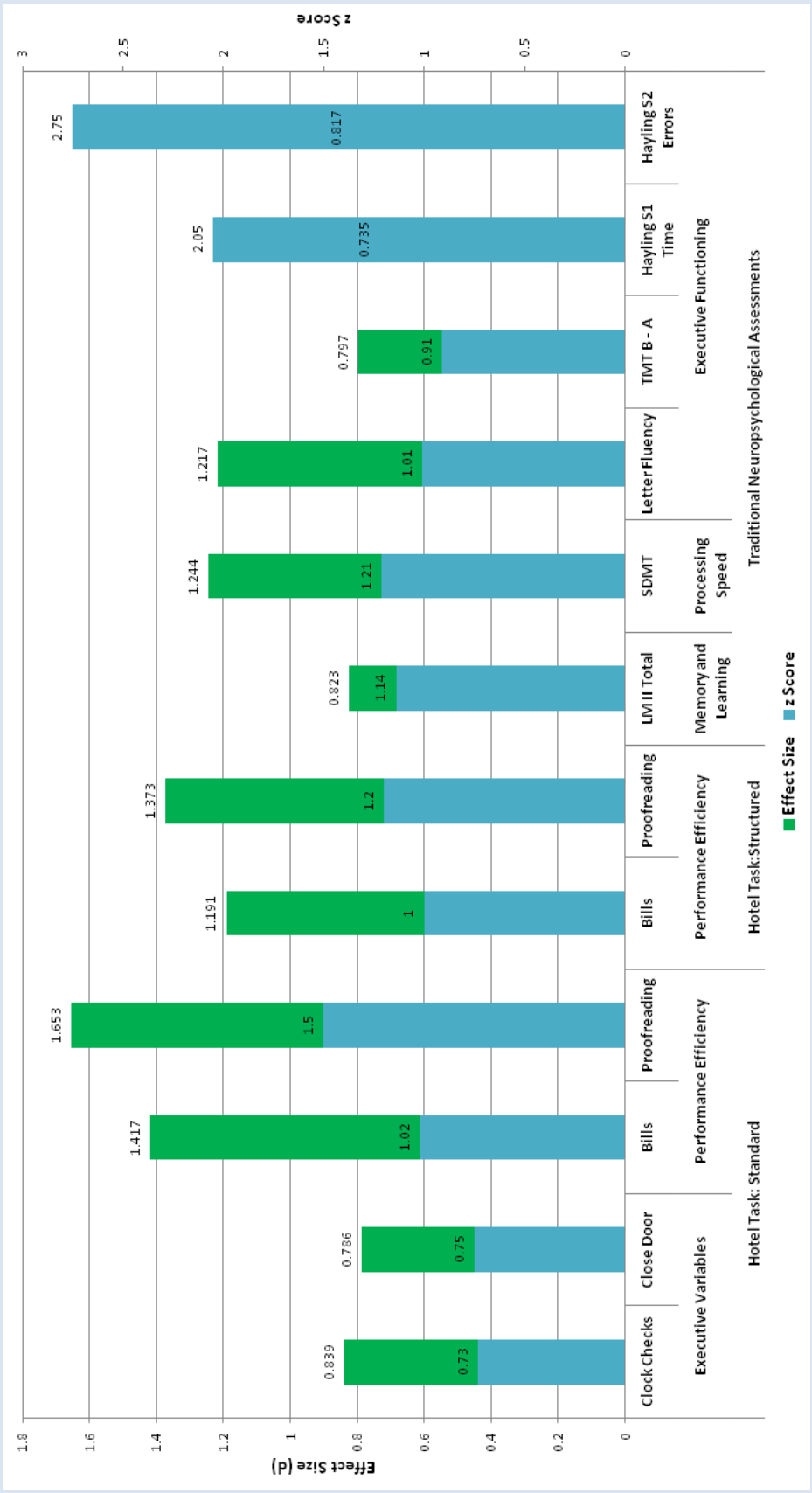


Figure 9: Comparison of the effect sizes and z scores for the Hotel Task and traditional neuropsychological tasks.

3.7.4 Hypothesis 4

This hypothesis predicted that performance on the Hotel Task will demonstrate greater sensitivity to the cognitive difficulties experienced by people with RRMS compared to traditional measures of executive functioning. This was assessed through comparison of the standardised scores for these tasks.

Figure 9 graphically compares the standardised scores for the Hotel Task and traditional neuropsychological tasks which were found to significantly differentiate the RRMS and healthy control groups. Looking first at the effect sizes (primary Y axis: green bar), it can be seen that the largest group difference was observed for performance efficiency on the Proofreading activity from the Standard condition of the Hotel Task (*d* = -1.653), with the Structured Hotel Task Proofreading activity showing the second largest effect size (*d* = -1.373). The highest effect size from the traditional neuropsychological tasks was the SDMT (*d* = 1.244). In contrast to the performance efficiency measures, the executive measures of the Standard Hotel Task (Clock Checks, *d* = -.839; Closing the Garage door time discrepancy, *d* = .786) had effect sizes more in line with the TMT B – A (*d* = .797) and Logical Memory II (*d* = .823) tasks.

With regard to the *z* scores (secondary Y axis: blue bar), it can be seen that the largest group difference was observed for the Hayling Task Section 2 Error score, following by the Total Time from Hayling Section 1. As noted above, this may relate to the low variance in performance of the control group on Section 1 Time (raw score variance = 8.70; range 0s to 9s) and Section 2 Errors (variance = 2.84; range 0 to 6 error points), compared to larger variation in performance of people with RRMS on this task: Section 1 Time (variance = 136.82; range 0s to 50s) and Section 2 Errors (variance = 59.48; range 0 to 25 error points). Considering the other variables, again the performance efficiency of the RRMS group on the Proofreading activity from the Standard version of the Hotel Task showed one of the largest *z* scores (*z*

= -1.5), higher than the SDMT (*z* = -1.21). The executive variables from the Standard condition of the Hotel task showed the lowest *z* scores of these variables (Clock Checks, *z* = -.73; Closing the Garage door time discrepancy, *z* = .75). If clinical impairment is defined as 1.5 standard deviations below the healthy control mean, the three tasks on which the RRMS group were clinically impaired were: Hayling Section 2 Errors (*z* = 2.75), Hayling Section 1 Time (*z* = -2.05) and Performance Efficiency on the Proofreading activity from the Standard condition of the Hotel Task (*z* = -1.5).

3.7.5 Hypothesis 5

The fifth (secondary) hypothesis related to the prediction that any impairments on the Hotel task and other neuropsychological variables cannot be better accounted for by levels of depression, fatigue or apathy. This prediction was tested by conducting ANCOVA analyses on the main variables, when adding the MFIS Total Score, CES-D score and FrSBe Current Apathy scale score as covariates. One difficulty with this approach is that the groups differed in terms of the covariates, indicating that these questionnaire variables are not randomly distributed across groups. Therefore adding the questionnaire data as a covariate may remove some of the shared group effect on neuropsychological performance (Miller & Chapman, 2001). Keeping this in mind, the analyses for this hypothesis were exploratory and caution was used when interpreting the results.

Using ANCOVA analysis, it was found that the effect of Group on Overall Performance Efficiency on the Standard Hotel Task was significant, even when self ratings on the MFIS, CES-D and FrSBe-Apathy subscale were held constant; $F(1, 36) = 8.765$, $p = .006$, partial $\eta^2 = .215$. In terms of Overall Performance Efficiency on the Structured version, again the effect of Group on this variance remained significant after controlling for self ratings on the questionnaires; $F(1,36) = 4.897$, $p = .034$, partial $\eta^2 = .133$.

In terms of the Hotel Task activities, a significant effect of Group was retained in the ANCOVA for time discrepancy with closing the garage door (Standard Condition); $F(1,36) = 5.615$, $p = .024$, partial $\eta^2 = .149$ and for Proofreading (Standard Condition) $F(1,36) = 9.221$, $p = .005$, partial $\eta^2 = .224$. In contrast, the effect of Group was no longer significant when the above covariates were added to the model for the following dependent variables: Clock Checks (Standard): $F(1,36) = 2.420$, $p = .013$, Proofreading (Structured): $F(1,36) = 3.544$, $p = .069$ and Compiling Bills (Structured): $F(1,36) = 4.937$, $p = .118$.

In terms of the traditional neuropsychological measures, the effect of Group on SDMT performance remained significant when the questionnaire data were added as covariates; $F(1,36) = 5.792$, $p = .022$, partial $\eta^2 = .153$. Similar results for found for Logical Memory II: $F(1,36) = 6.835$, $p = .014$, partial $\eta^2 = .176$. The effect of Group did not retain significance when the questionnaire data were added as covariates to the model for the following dependent variables: Letter Fluency; $F(1,36) = 3.737$, $p = .062$ and TMT B-A; $F(1,36) = 1.315$, $p = .260$.

ANCOVA analyses were not conducted on the remaining variables as these were either found to not differ between groups or were not appropriate for parametric analyses.

3.7.6 Hypothesis 6

The final, exploratory hypothesis related to the ability of the Hotel Task variables to predict cognitive difficulties in everyday life, in particular executive dysfunction. Everyday cognitive difficulties were operationalised using the following dependent variables: the Executive Dysfunction scale from the FrSBe and IADLs as rated by a family member or other informant. As the self and family ratings were not found to significantly differ within participants, self rated Executive Dysfunction was used.

Performance data on the main Hotel Task variables were entered into an ANCOVA model in order to assess how well it accounts for variance in current self rated FrSBe Executive Dysfunction scores. Looking at overall time discrepancy scores, this variable was not found to be predictive of self rated executive functioning for both the Standard condition of the Hotel Task; b = 1.272, $t(36)$ = .979, p = .334, and the Structured condition; b = 1.173, $t(36)$ = 1.611, p = .116. Overall Performance Efficiency (Standard condition) did not significantly predict self rated Executive Dysfunction scores; b = -1.557, $t(36)$ = -.797, p = .431, with similar results for Overall Performance Efficiency (Structured condition); b = -2.469, $t(36)$ = -1.454, p = .155.

These analyses were repeated using the activity from the Hotel Task which was most sensitive to group differences: Proofreading the Hotel Leaflet. In terms of performance efficiency, Proofreading from the Structured condition was found to predict self reported executive functioning in daily life; b = -2.311, $t(36)$ = -2.686, p = .011, r^2 = .135; however efficiency on the Standard condition Proofreading activity was not a significant predictor; b = -1.189, $t(36)$ = -1.507, p = .141.

The relationship between IADLs and neuropsychological task performance was explored using Spearman's Rho non-parametric correlation. Note that IADL ratings were available for 16 RRMS participants only. Informant rated IADLs were not found to be significantly correlated with the main Hotel Task variables. Of the traditional neuropsychological tasks, IADLS correlated with Letter Fluency performance only; ρ = -.632, p = .009. IADLs also significantly correlated with GNDS-LL score; ρ = .633, p = .008 and working status; ρ = -.599, p = .014. There was no significant correlation between IADL and MOCA score; ρ = -.220, p = .412.

3.8 Summary of Findings

In summary, the RRMS participants were found to be impaired at a group level on several of the background neuropsychological tasks, including measures of executive functioning such as Letter Fluency, TMT and the Hayling task; as well as on other neuropsychological measures, in particular the SDMT and Logical Memory.

In addition, participants with RRMS were found to significantly differ from healthy controls on some executive variables from the Standard condition of the Hotel task, including number of clock checks and discrepancy from the optimal time for closing the garage door. The largest group differences were observed for performance efficiency on the Proofreading and Compiling Bills activities from both conditions of the Hotel Task. Notably, there was no evidence of an interaction between group and condition in terms of either overall time discrepancy and overall performance efficiency on the Hotel Task, with participants with RRMS performing equally poorly across both conditions.

RRMS group impairments on some Hotel Task measures did not disappear when questionnaire measures of fatigue, depression and apathy were added as covariates. Generally, Hotel Task variables did not predict self reported executive functioning, nor did they correlate with informant reported IADLs. These results will be interpreted in the following chapter.

4 Discussion

4.1 Summary of the Current Study

The current study aimed to investigate cognitive difficulties associated with RRMS using a novel adaptation of a neuropsychological task of executive functioning designed to be ecologically valid, the Hotel Task. Participants with RRMS and healthy control participants completed this task across two conditions: a 'Standard' condition with high executive demands, and a 'Structured' condition with lower executive demands. Specifically, this task places demands on multitasking, planning, switching, monitoring and prospective memory abilities. The two groups also completed a selection of background neuropsychological assessments and relevant questionnaires.

This chapter will summarise the findings of the current study, and interpret these in light of the previous literature. The methodology of current study will then be critically assessed, with an appraisal of methodological strengths and limitations. The implications of the current findings will then be proposed; relating these results to the current understanding of cognition in MS and considering clinical implications. Finally, recommendations for future research on cognition in RRMS will be suggested, and the overall conclusions of the study will be presented.

4.2 Summary of Findings

4.2.1 Representativeness of Sample

In terms of the background neuropsychological assessments, the participants with RRMS were found to have a cognitive profile similar to that described in previous research. In particular, participants were found to display significantly reduced performance on tasks of processing speed, verbal learning and some

standard assessments of executive functioning. Participants were also relatively similar to previous samples of people with RRMS described in the literature in other ways: having relatively mild physical disability, high levels of fatigue, a high rate of self reported depression and on average receiving a diagnosis of MS ten years ago. In terms of self reported impact, members of the RRMS group were also more likely to emphasise the impact of physical symptoms and fatigue on their work and other roles compared to the impact of cognitive difficulties, in keeping with previous research (e.g. Smith & Arnett, 2005).

4.2.2 Hypothesis 1

"Participants with RRMS will perform poorly in terms of the executive variables on the high executive demand (Standard) condition of the Hotel Task relative to healthy control participants, if executive abilities are compromised in RRMS."

The results partially supported this hypothesis. Participants with RRMS looked at the clock significantly less often than members of the healthy comparison group, and this group difference was classified as a 'large' effect size. This may indicate difficulties in task monitoring, as well as dividing attention between different demands. Monitoring the time was also necessary to successfully complete the prospective memory tasks: to remember to 'open' and 'close the garage doors' at specific times by pressing a button. Participants with RRMS had significantly greater time discrepancies from the specified times for the second button press ('closing the door') compared to healthy controls, with a 'moderate' effect size. The groups did not differ in terms of time discrepancy for the first button press.

No other group differences were noted on the other 'executive' variables on the Standard condition, including no difference in terms of tasks attempted or time discrepancies from the optimal time for the five ongoing Hotel Task

activities. Group differences on two of these variables approached, but did not meet, significance (Total Score and the Compiling Bills activity).

4.2.3 Hypothesis 2

"Participants with RRMS will show fewer deficits on the main Hotel Task variables in the lower executive (Structured) version of the Hotel Task, compared to the Standard version."

This hypothesis was not supported. In the Structured condition, participants were given the same instructions as in the Standard condition, but were provided with a plan and external prompts to switch tasks and complete actions. Across both conditions of the Hotel Task, participants with RRMS were found to perform poorly compared to healthy control participants, with no significant interaction between group and condition noted for overall standardised time discrepancy scores. While the effect of condition was not significant, the effect of group was statistically significant. Participants with RRMS performed approximately one standard deviation worse than the control group on both conditions for this overall time discrepancy score ('Standard' condition = .89 SD, 'Structured' condition = 1.14 SD). Looking to the descriptive data, it can be seen that both groups showed time discrepancies closer to zero during the Structured condition, although control participants maintained better performance than people with RRMS across conditions, with less variance in performance amongst control participants. This suggests that people with RRMS as a group do not experience a prominent impairment in some areas of executive functioning, as reducing the executive demands of the task does not disproportionally improve performance compared to controls. This will be discussed further below.

4.2.4 Hypothesis 3

"Participants with RRMS will demonstrate reduced performance efficiency on both conditions of the Hotel Task compared to controls, reflecting lower level cognitive impairments such as slowed information processing speed."

This hypothesis was supported. In terms of performance efficiency, the actual ability of participants to complete items of the Hotel Task activities within one minute, participants with RRMS performed poorly compared to healthy control participants in both conditions of the task. With regard to the overall standardised performance efficiency score, this difficulty was equally observed in both the high and low executive demand conditions: Standard condition = -1.38 SD, Structured condition = -1.43 SD. This pattern of relative impairment was also observed across all five component activities. This is consistent with the interpretation that participants' impairments were not attributable to specific impairments in executive functioning, nor was a decrease in executive demands sufficient to result in a statistically significant improvement in overall performance efficiency on the Hotel Task.

Looking at the activities in turn, the activities which participants with RRMS struggled with most were 'Proofreading the Hotel Leaflet' and 'Compiling Customer Bills'. These tasks primarily involve visual search and processing speed demands, with a motor (written) response. Other tasks varied in their ability to differentiate groups, and this may relate to a combination of specific cognitive demands of tasks and task difficulty. For instance the activity involving sorting coins into bags of a specific value (£1) did not differentiate groups in either condition, despite requiring a motor response, while both groups performed poorly on the directory search task in the Structured condition, resulting in a 'floor' effect.

One could argue that the executive and performance efficiency variables both rely on a combination of lower and higher level processes. For example, if participants do not generate and implement a plan effectively, they may not

attempt a particular activity, resulting in a performance efficiency score of zero. However, in the Structured condition, all participants attempted all tasks, and the group difference in efficiency remained significant. Furthermore, performance efficiency scores were standardised, by calculating how many items participants would have correctly completed in 60 seconds, regardless of whether less than or more than 60 seconds was spent performing the task.

This suggests that the combination of difficulties experienced by people with RRMS lead to reduced functioning on some of the types of administrative activities included in the Hotel Task, and this reduction in output is similar regardless of whether support with planning and time monitoring is provided. Again, there was greater variance within the RRMS group compared to the healthy control group, suggesting that people with RRMS varied more than controls in their ability to benefit from the support provided.

4.2.5 Hypothesis 4

"Performance on the Hotel Task will demonstrate greater sensitivity to the cognitive difficulties experienced by people with RRMS compared to traditional measures of executive functioning."

The current findings partially corroborated this hypothesis. Comparing the effect size of the difference between groups across tasks, the largest effect sizes were seen for performance efficiency on the two most sensitive activities of the Hotel Task: Compiling Bills and Proofreading the Hotel Leaflet in the Standard condition. These effect sizes were larger than those seen on traditional executive functioning tasks and other neuropsychological tasks, including the SDMT and letter fluency task. This would suggest that the cognitive difficulties experienced by people with RRMS are most noticeable in terms of efficiency of performance on tasks requiring paced performance on visual search, in the context of more demanding situations requiring planning, monitoring, switching and prospective memory. In contrast, the executive

variables from the Standard Hotel Task (number of clock checks and button press time) were not better able to detect the difficulties of people with RRMS compared to traditional neuropsychological assessment tasks.

Standardised *z* scores were also calculated, as an index of the performance of people with RRMS relative to the control group. The performance of the RRMS group is expressed as the number of control group standard deviations below the control mean. For most tasks, the profile of *z* score data was similar to the effect size data, and again the Compiling Bills and Proofreading tasks from the Standard condition demonstrated sensitivity to group differences relative to other tasks. Additionally, the Hayling Sentence Completion Task differentiated the groups clearly and in fact this task was associated with the largest *z* score differences of any variables. There was a large difference between groups on two of three *z* score variables (Section 1 time and Section 2 error score), with the RRMS group performing over two standard deviations below controls. Section one of the Hayling task involves initiation, and also requires processing speed in that participants are expected to respond quickly. Section two of this task involves inhibition of previously well learned responses. These relatively large *z* scores may relate to the task demands, in that most control participants displayed similar and unimpaired performance on these variables, while the group of people with RRMS showed a much wider variance in performance. For instance, the response times of participants with RRMS on Section 1 ranged from zero seconds to 50 seconds, while the corresponding range for the healthy controls was zero to nine seconds.

Overall, the current study provides preliminary evidence that the Hotel Task is sensitive to the cognitive difficulties experienced by people with RRMS, and in particular when performance efficiency is considered.

4.2.6 Hypothesis 5

"Neuropsychological task impairments will remain significant when symptoms of depression, fatigue and apathy are statistically controlled for."

There was some support for this secondary hypothesis. The results from the current study suggest that some group differences were retained, even once differences in self reported mood, fatigue and apathy were accounted for. In effect, this means that even when participants obtained the same score on questionnaires of depression, fatigue and apathy, the group with RRMS continued to perform significantly worse on the following four variables: overall performance efficiency on the Standard and Structured Hotel Tasks, Closing the Garage Door (Standard condition) and Proofreading (Standard condition). Keeping in mind the inherent difficulties in statistically 'controlling' for a variable which is not randomly distributed across groups, these results should be interpreted with caution. Nonetheless, these data suggest that some group differences remain significant, even after variance which may be shared between questionnaires and Hotel Task variables is 'removed'. This would suggest that these factors are not sufficient explanations of the group differences observed in the current study.

4.2.7 Hypothesis 6

"Hotel Task performance will be associated with cognitive difficulties in daily life, as indexed by self reported executive dysfunction and informant rated instrumental activities of daily living."

This hypothesis was not supported. Ecologically valid assessments were developed in order to better predict functioning on everyday cognitive tasks in real world settings. As such, the performance of participants on the Hotel task was compared to self and informant reported functioning in daily life. The only Hotel Task variable which was found to statistically predict self reported Executive Functioning (from the FrSBe Executive Functioning subscale) was

performance efficiency on the Proofreading task (Structured condition), and this accounted for only 13.5% of the variance in questionnaire scores. It is notable that the executive measures from the original Hotel Task did not predict everyday executive functioning.

Correlational analyses indicated that there was no significant association between performance on the Hotel Task and informant rated IADLs. The only traditional neuropsychological task which correlated with IADLs was verbal fluency. In contrast IADLs were related with self rated reports of functioning, for example mobility impairments and working status.

4.3 Overview of Findings and Comparison to Previous Literature

4.3.1 Main Hypotheses

Contrary to the prediction that people with RRMS will have prominent difficulties on cognitive tasks with higher executive demands, the results indicated that people with RRMS did not have pervasive difficulties with planning and switching, and that across both conditions of the task they displayed less efficient performance compared to the healthy comparison group. To our knowledge, no previous research has compared high and low executive demand conditions on the Hotel Task with a sample of people with MS in a single study. However previous research has suggested that people with RRMS are frequently impaired on tasks which primarily place demands on executive functions (e.g. Drew et al., 2008; Godefrey et al., 2010), and there has been some suggestion that lower level deficits in abilities such as processing speed are not sufficiently able to explain difficulties on executive functioning tasks (e.g. De Sonneville et al., 2002).

In keeping with the findings of Roca and colleagues (2008), the current study found that participants with RRMS had significantly greater difficulty with the prospective memory component of the Hotel Task than healthy controls. Roca's study found that participants with RRMS differed from healthy controls

in the “button deviation times”, although this variable combined both button press actions (‘opening’ and ‘closing’ the garage door). The current study also observed a significant difference in time monitoring (number of clock checks) between groups, but this variable was not reported in Roca’s study. Both the current study and Roca’s study found that all healthy control participants pressed the buttons twice, while this was not true of the MS groups. These difficulties in prospective memory and time monitoring are also reflected in previous studies which used other tasks, such as the Virtual Week task (e.g. Rendell et al., 2007). No other significant findings were found for the executive variables in Roca’s study, and this finding was replicated in the current study.

In terms of performance efficiency, a novel outcome variable recorded in the current study, the current findings are in keeping with the consensus from previous research that people with RRMS perform more slowly than healthy controls under timed conditions across many task types. Interestingly, no significant group differences were found on only one activity from the Hotel Task in either condition (Sorting Coins), although there was a trend towards participants being slower on the Structured version of the task.

Looking to other research studies which have used the Hotel Task with different populations, a different pattern of difficulties is noted. While the current study observed similar performance across groups on the planning and multitasking aspects of the Hotel Task, research with people with acquired brain injury (Manly et al., 2002) and fronto-temporal dementia (Torralva et al., 2009) found significant impairments on these executive variables. For example, Torralva’s study found that ‘high functioning’ people with fronto-temporal dementia (as measured by a cognitive screening instrument), were impaired on deviation from the optimal time per activity, indicating planning difficulties, and this was in the context of few difficulties on traditional neuropsychological tasks. Furthermore, the Hotel Task appears to have reasonable face validity as an assessment of planning and multitasking.

As such, the lack of significant group differences on the executive variables of the Hotel Task in the current study are likely to relate to characteristics of RRMS, rather than the Hotel Task being a poor detector of these difficulties.

Finally, the current study found some evidence that the Hotel Task, developed to capture aspects of complex everyday cognitive tasks, was more sensitive to the broader cognitive difficulties experienced by people with RRMS compared to traditional neuropsychological tasks in a clinic setting. This was observed in particular for performance efficiency on the activities involving visual search, focused attention and speed of processing. This is in keeping with previous studies which have suggested that tasks developed to be more representative of everyday activities are sensitive to MS related cognitive impairments. For example, previous studies have observed difficulties on the MET as well as the Hotel Task (Roca et al., 2008), in addition to difficulties on the TEA and RBMT (Higginson et al., 2000). However, it is important to note that performance deficits on measures such as the SDMT and PASAT, as indexed by *z* scores, were greater in magnitude than deficits on the RBMT and TEA in Higginson's study. In contrast, the current study found that efficiency of performance of people with RRMS on some activities during the Hotel Task was more impaired than performance on the SDMT.

4.3.2 Secondary Hypotheses

While not the focus of the current study, there was some evidence that the observed impairments were not explainable in terms of the effects of non-cognitive variables on cognition. The current study found that levels of fatigue, depression and apathy were not sufficient to account for the observed group differences on several of the Hotel Task variables. This was generally in keeping with previous findings comparing neuropsychological performance and subjective reports on questionnaire measures of these variables.

In terms of fatigue, the general consensus from previous research is that subjectively reported fatigue does not correlate with neuropsychological test performance (e.g. Chiaravalloti & DeLuca, 2008). This is not to say that the effects on people with RRMS of sustained cognitive effort over the current testing session, lasting 90 minutes, did not contribute to reduced performance (e.g. Krupp & Elkins, 2000). Similarly with regard to mood, subjective reports of depression have typically not been found to be associated with neuropsychological test performance (e.g. Julian et al., 2007), although depression may be significant in other ways, for example as a predictor of later cognitive decline. Finally, few previous studies have considered the association between apathy and cognition in RRMS, with one study reporting that apathy, as measured by the FrSBe, is associated with performance on effortful neuropsychological tasks in MS (Chiaravalloti & DeLuca, 2003). However, Chiaravalloti's study found that the group with RRMS and healthy controls differed only with regard to performance on the PASAT, indicating a less cognitively impaired sample compared to the current study. Chiaravalloti's study also used correlational methods, and did not investigate the relative contributions of apathy and other factors to neuropsychological task performance.

The final hypothesis related to the predictive power of the Hotel Task variables in terms of self- and informant-rated cognitive functioning in daily life. This study found little support for this hypothesis, with only the performance efficiency variable for Proofreading (Structured condition) found to predict subjective ratings of executive functioning in daily life. This is at odds with previous research, which found an association between functional disability in daily life and ecologically valid measures of memory and attention (Higginson et al., 2000). However, it is important to note that 'everyday cognitive functioning' was indexed in the current study using only two questionnaire measures (the Executive Functioning scale of the FrSBe and the IADL scale), and as such, these results should be interpreted with caution.

4.4 Methodological Issues

The following section will detail some of the methodological strengths and limitations of the current study, with a focus on ways in which the current study extended previous findings, as well as identifying limitations to be addressed in future research.

4.4.1 Strengths

The primary methodological strength of the current study related to the adaptation of a measure of executive functioning, the Hotel Task, in order to attempt to unpack the relative contribution of higher level (executive) and lower level cognitive difficulties associated with RRMS to reduced performance on aspects of complex, everyday tasks. Previous studies using neuropsychological tests of executive functioning have generally been limited in that it is difficult to say if the observed reduction in performance is due to a combination of difficulties in executive and lower level abilities, or mostly accounted for by lower level difficulties. By administering the Hotel Task in two conditions, which manipulated the executive demands of the task, and by recording data on how well people with RRMS performed in addition to how well the rules were followed, the current study was able to go some way to explore this issue in MS research.

A second main strength of the study related to the inclusion of both the modified Hotel Task and a range of background neuropsychological measures. This allowed the clinical sample to be described in terms of performance on a traditional battery of assessments, and also allows performance on the Hotel Task and traditional neuropsychological tasks to be directly compared within the same sample. Given the complex nature of the Hotel Task, one potential difficulty is identifying the main underlying impairments contributing to poor performance. In the current study, this difficulty was addressed by considering the findings from the Hotel Task in light of the performance of the sample on more circumscribed traditional

tasks. Furthermore, in the current study, the performance of the sample of people with RRMS on the background tasks indicated a similar cognitive profile to previous samples. This suggests that the observed difficulties on the Hotel Task are likely to be representative of people with RRMS at the population level. Additionally, using this methodology the relative sensitivity of the Hotel Task to commonly used neuropsychological measures could be compared, with the goal of assessing whether there is an advantage to using the Hotel Task in assessing cognition in RRMS.

Other strengths of the current methodology include consideration of non-cognitive factors which may affect performance on neuropsychological tasks, as well as restricting recruitment to a single MS subtype in order to maintain study integrity.

4.4.2 Limitations

The main limitation related to sample size and statistical power. Greater statistical power decreases the probability of failing to detect a true group difference; reducing the likelihood of Type II errors. The power analysis conducted when designing the current study indicated that 23 participants were needed in each group in order to achieve 80% statistical power to detect a group difference at the 5% significance level. This figure was calculated based on the 'Button Deviation Times' from the only previously published study to administer the Hotel Task to people with RRMS (Roca et al., 2008). The current study included a final sample of 19 people in each group, and thus, it could be argued that the study is slightly underpowered with regard to detecting group differences on button deviation times.

However, it is important to note a number of issues when considering the power analysis. The current study detected a group difference on one of the button time deviation variables, suggesting that sufficient power was achieved, while a small effect size was noted for the other button variable.

Roca's study analysed data based on a variable which combined the first and second button press time deviations, although it is unclear from the paper the exact method used to calculate this value. Nonetheless, the effect size obtained by Roca for the overall button deviation time value was similar to the effect size observed in the current study for the second button press time deviation.

More generally, the current study observed clearly significant group differences on some Hotel Task variables, typically when effect sizes were in the 'large' range or upper part of the 'moderate' range. Additionally, there was a trend towards significance for some dependent variables even though they were not found to significantly differ between groups. Looking at effect sizes, these typically fell in 'moderate' effect range. The main examples are overall executive *z* score on the Standard Hotel Task (*d* = .631) and Compiling Bills from the Standard Hotel Task (*d* = .641). In order to ensure the study had 80% power to detect the smaller of these effect sizes, a sample size of 32 per group would be needed, and it was beyond the scope of the current study to recruit and assess this number of participants. This issue should be addressed in future research using the Hotel Task, to increase confidence that significant group differences were not missed. The current sample size was also comparable to the modest sample sizes used in other studies investigating neuropsychological functioning in people with RRMS.

Secondly, while the groups were not found to significantly differ in terms of relevant variables (gender, age, estimated premorbid intellectual functioning and years in full time education), closer investigation of the descriptive data suggest that the RRMS group tended to have a larger range in age and ability, and with a slightly different profile compared to the healthy controls. In particular, the control group included more people with a greater number of years of full time education compared to the RRMS group, and this was reflected in the slightly higher estimated FSIQ of the control group. In order to minimise the possible confounding effects of differences in cognitive ability

and education, the data of two participants were removed from the final analyses: the participant with the lowest estimated FSIQ in the group with RRMS and the participant with highest estimated FSIQ in the control group. No significant group difference on these variables was noted in the final sample.

A final limitation to the study related to task order. A decision was made to administer the tasks in an identical order for all participants. In terms of the neuropsychological tasks overall, this was to ensure that participants would complete the tasks considered to be most vital to the hypotheses first. In the current study, the order effects were consistent for both groups, and thus these effects were controlled for by comparing performance between the two groups. One exception to this may have been the effects of fatigue, in that people with RRMS are more likely to experience fatigue during sustained cognitive effort than healthy control participants (Krupp & Elkins, 2000). However, the relatively short duration of the research session (90 minutes), compared to four hours in the above study, was likely to minimise the effects of fatigue, for both experimental and ethical reasons. While fatigue was not measured before and after the tasks, all participants completed the whole battery of tasks and participants rarely accepted the offer of a break, suggesting that participants did not experience a significant level of fatigue.

With regard to the Hotel Task, the two conditions were administered in a set order. Administering the Structured Condition before the Standard Condition was avoided as this would invalidate the task, in that participants would likely recall the recommended plan and implement this, rather than generating a plan independently on the Standard Condition. In terms of the component activities, these were presented to participants in a consistent order when giving the task instructions for both conditions. It was not possible to control the order of tasks in the Standard condition, as participants were required to draw on their own organisational abilities in response to the task rules. In the Structured condition all participants were given the same ‘Recommended

Plan' which included suggested task order, and this was to facilitate the administration of the task. Therefore, it is possible that task order effects may have affected the current results. However, by including a comparison group and by prompting participants to change task at predefined time points during the Structured condition, many of these effects are accounted for or held constant between groups, minimising the confounding effects as much as possible while maintaining ecological validity.

4.5 Theoretical Implications

In terms of theory, this section will consider implications for the overall understanding of executive functioning difficulties in RRMS, the status of prospective memory in RRMS and finally implications for the "Relative Consequence Model".

4.5.1 Executive Functioning and Prospective Memory

Considering the aspects of executive functioning involved in successful completion of the Hotel Task, including multitasking, planning, monitoring, inhibition and switching, the results of the current study suggest that people with RRMS do not have a specific and pervasive difficulty with executive functioning that is disproportionate to difficulties in lower level abilities, such as processing speed and verbal memory. This interpretation is based on the lack of a significant effect of condition in the Hotel Task, as participants performed as poorly compared to controls in the low executive demand condition as they did in the high executive demand condition.

Within executive functioning, this study did find evidence of a specific difficulty with prospective memory, in keeping with the results of previous studies (Kardiasmenos et al., 2008; Rendell et al., 2007), and in particular previous tasks involving clock monitoring to complete a time based action (Rendell et al., 2012; Roca et al., 2008). An alternative explanation of this finding may be that participants had difficulties with delayed recall of information leading to

forgetting this part of the task instructions, as the group with RRMS were significantly worse on delayed recall of verbal information. However, attempts to reduce the contribution of poor retrospective memory were made by requiring participants to repeat the task instructions satisfactorily prior to starting the task, as well leaving written reminders of instructions in front of participants throughout both conditions.

Prospective memory typically occurs without an external request or prompt to remember, and involves switching attention from the ongoing task to the intended action in order to perform it. The multi-process model of prospective memory states that this form of memory can be achieved through a number of different processes, in particular a combination of more strategic, effortful processes and relatively automatic, less resource demanding processes (McDaniel & Einstein, 2000). Interestingly, participants with RRMS did not differ from controls for the first button press (six minutes into the task), but tended to have greater time deviations for the second button press (12 minutes into the task) compared to controls. One possible explanation for this is that the intention of participants to press the button was strongest at the beginning of the task, as participants relied on relatively effortful, strategic processes in the first instance. For example, this may involve frequently checking the time for cues as to when to press the button and frequently bringing the intention to mind.

This intention may have lessened in strength in the context of competing task demands after participants had completed the required action once, and thus a switch was made to relying on relatively automatic processes for the second button press. This switch may have been maladaptive for people with RRMS as it was associated with a reduction in time monitoring, and may explain participants with RRMS performed poorly on this second action. Consistent with this possible explanation is that people with RRMS monitored the time less frequently overall than healthy control participants, and six participants from the RRMS group did not press the button on the second occasion at all.

It is also of note that all participants pressed the buttons during the low executive demand task, when external prompts to switch tasks were given (even though specific prompts to press the buttons were not mentioned).

4.5.2 Relative Consequences Model

The 'Relative Consequence Model' states that the cognitive difficulties observed in RRMS can be explained by a pervasive reduction in processing speed impacting on the performance of many different tasks. It was noteworthy that many of tasks in the current study that were sensitive to cognitive difficulties in the RRMS group involved timed performance (e.g. generating words in a limited time, timed completion of sequencing and switching tasks, response speed on a low demand verbal task) or limited presentation of verbal information (delayed verbal recall). Similarly, the observed reductions in performance efficiency on the Hotel Task could be explained by reduced speed of information processing in combination with slowed motor response speed. However, slowed processing speed is unlikely to fully account for the observed difficulties in prospective memory, nor is this a full explanation of why participants with RRMS made significantly more errors on Section 2 of the Hayling Task. Therefore, in keeping with previous studies (DeSonneville et al., 2002; Parmenter et al., 2007), the current findings suggest that while processing speed difficulties are likely to have a large effect on neuropsychological task performance, slowed information processing is not a sufficient explanation for the observed profile of difficulties.

4.6 Clinical Implications

This section will consider the recommendations for clinical practice which arise from the current results, in particular focusing on cognitive assessment, cognitive rehabilitation and employment support.

4.6.1 Cognitive Assessment

The primary findings of the current study suggest that using a neuropsychological assessment which reflects aspects of complex, everyday activities can be more sensitive (on some outcomes) than traditional neuropsychological assessments. As such, one recommendation from this study is to include more of these complex tasks of cognitive functioning alongside currently used and well evidenced neuropsychological batteries. This may facilitate detection of cognitive difficulties which may not be easily detected by traditional measures, but may impact on people's functioning in daily life.

However, the advantages of using the Hotel Task in a clinic setting need to be balanced against the disadvantages. The Hotel Task, as described by Manly and colleagues, takes over 20 minutes to administer. It involves multiple test materials, and takes some time to set up and to score. In contrast, robust traditional neuropsychological tasks, such as the SDMT and letter fluency, can be quickly administered with few materials. Therefore, the Hotel Task may not be suited to cognitive screening in a busy clinic environment. Secondly, while poor performance on the Hotel Task may indicate that the examinee has difficulty with complex cognitive tasks, it does not typically provide information on the specific nature of the difficulty. For example, given the heterogeneity of cognitive difficulties in RRMS, it may be that poor performance indicates pervasive difficulties in one individual, while for another person the difficulties may be due to a specific problem with processing speed, or planning. As such, it should be used alongside other neuropsychological tasks which can provide information about specific cognitive difficulties. Therefore, use of tasks such as the Hotel Task may be best suited to hypothesis driven assessments, for example where an individual reports cognitive difficulties in daily life but performs normally on typical screening measures. The Hotel Task may also be advantageous when considering cognitive rehabilitation, for example as a method of assessing

whether the use of cognitive strategies has been beneficial on an individual basis.

Additionally, the current results are consistent with previous findings that people with RRMS are more likely to experience difficulties on prospective memory tasks. In the clinic, patients may often describe these difficulties under the heading of 'memory problems' and so it may be helpful to consider whether prospective memory is impaired, even when other forms of memory appear intact on neuropsychological assessment measures. The Hotel Task may be helpful in the initial assessment and evaluation of rehabilitation interventions for prospective memory difficulties.

4.6.2 Cognitive Rehabilitation and Employment Support

The results of the study with regard to prospective memory suggest that this could be a beneficial area of focus in future research on cognitive rehabilitation in RRMS. For instance, difficulties with remembering to do something in the future could lead to forgetting to take medication consistently or attend medical appointments without support. It would also likely have a significant impact on workplace functioning, across many different types of jobs. Further research is needed on how prospective memory problems may present in daily life for people with MS (Rendell et al., 2012). However, a previous study has found that forming stronger "Implementation Intentions" was an effective strategy to improve prospective memory performance in people with MS in the laboratory (Kardiasmenos et al., 2008). This study involved instructing participants to initially take the time to imagine completion of the target action alongside stating the intention to complete this as an "if... then..." statement.

One rationale for this study related to investigating the performance of people with RRMS on complex, everyday tasks with the goal of developing recommendations to assist people who decide to remain in employment or

return to employment. Employment has been identified as an important contributor to social functioning and quality of life (e.g. Bevan et al., 2011). Overall, this study did not suggest that providing people with RRMS with a plan to organise their activities or prompts to switch task led to an increase in efficiency of performance. While this study had a modest size, this would indicate that providing greater managerial support, or training people with MS to better plan and organise their time, may not lead to improved performance or functioning (with the exception of prospective memory tasks, discussed above). Rather, rehabilitation efforts may be better targeted at reducing the effects of impaired processing speed and related difficulties, for example focusing on adjusting the balance between speed and accuracy in order to achieve a goal. Additionally, the current findings may be helpful in providing employers with practical information about the nature of cognitive difficulties in RRMS, and support the recommendation that additional time be allocated to complete tasks, as a reasonable accommodation in the context of RRMS.

4.7 Future Research

Recommendations for future research will be discussed in terms of addressing the limitations of the current study, further research on the Hotel Task with people with MS, and areas of executive functioning which may be useful targets for future research.

Further research using the Hotel Task with people with MS, using the novel Structured condition described here, would be beneficial. Any replications of the current study would benefit from recruiting a larger sample size, in order to reduce Type I error and increasing confidence in the statistical findings. A sample size of 34 to 40 participants per group would be recommended at a minimum, in order to improve statistical power to detect possible group differences on some Hotel Task measures. Furthermore, it would be beneficial to implement a tighter participant matching system, to increase the likelihood that participants with RRMS and healthy controls do not differ

except in relation to MS symptoms and related functional impacts. It may also be beneficial to randomise task order, in an attempt to control for any task order effects in a more experimental manner. For example, the locations of the activity materials for the Hotel Task could be counterbalanced, as could the activity order in the Recommended Plan sheet. Alternatively, in a larger sample order effects could be assessed by randomly assigning participants with MS and controls to different groups who complete the tasks in different orders.

The results of the current study indicated that some Hotel Task activities were more impaired in people with RRMS compared to controls. These activities were selected to represent everyday activities, such as administrative tasks from the work place. It would be helpful to consider the properties of these activities in more detail in future research, for example adjusting task difficulty to minimise the risk of floor or ceiling effects (as observed for the Directory Search task). It may also be that some of these 'pencil and paper' activities are now less commonly required in the workplace. As such, the Hotel Task activities could be adjusted to reflect this, for example by combining paper based and computerised tasks, or developing a computerised version of the Hotel Task. One example of this may be to replace the Directory Search task with an internet search task, where participants are requested to record the contact details of the cheapest service they can find (e.g. florist, emergency locksmith). Furthermore, it would be helpful to investigate whether a shortened version of the Hotel Task, standardised for use in people with MS, would also detect cognitive difficulties.

Future research using the Hotel Task could also investigate the performance of people with different subtypes of MS and with different disease duration or characteristics on the Hotel Task. One prediction from previous research is that cognitive impairments can become more pervasive over time and in the progressive forms of the disease. (e.g. Amato et al., 2001). This could be investigated in terms of performance on the executive and performance

efficiency variables of the Hotel Task, with the prediction that Secondary Progressive MS is more likely to be associated with impaired performance on this task. Further research on the impact of mood and apathy on Hotel Task performance could experimentally control for these variables, for example by assigning participants with RRMS to 'low mood' and 'normal mood' groups and comparing performance (e.g. Arnett et al., 2001).

In terms of future research on executive functioning in MS more generally, the results of this study would indicate two main directions. Firstly, future research on prospective memory in MS would be warranted, with a particular focus on comparing different processes which may underlie prospective memory. In particular, it would be of interest to compare the performance of people with MS on more strategic prospective memory processes and performance on more automatic processes, across both time based triggers (as in the Hotel Task) and event based triggers (such as seeing a cue which serves as a reminder of an intended activity).

A second direction for future executive functioning research in RRMS is to explore in more detail the relationship between everyday functioning and performance on ecologically valid tests of executive functioning, such as the Hotel Task, BADS and MET. More focused and robust research on this relationship may benefit from including different sources of information regarding everyday functioning, such as a more comprehensive selection of indices of functioning such as detailed employment variables, self and informant rated questionnaires, semi-structured interviews and direct observations in daily activities. It would be useful to also administer a battery of conventional neuropsychological assessments alongside these measures to further explore the relative utility of the *versidicality* approach (investigating the predictive power of established neuropsychological tasks) and *verisimilitude* approach (developing newer tasks to better represent everyday activities) to ecological validity research within the context of MS research.

4.8 Summary and Conclusion

There have been many recent studies which have investigated cognition in MS. These studies have frequently led to mixed findings, particularly with regard to assessments of executive functioning. Some of this heterogeneity is increasingly being understood by considering disease factors, such as disease subtype and duration. More recently, there has been a consensus from the literature that there is a 'typical profile' of cognitive difficulties in MS, although there are many questions unanswered such as the relatively contribution of lower level and higher level abilities to poor task performance.

The current study investigated the status of some abilities within executive functioning and cognitive abilities more generally in RRMS. The results indicated that people with RRMS display impaired performance on a complex task, designed to be more ecologically valid, in terms of efficiency across both high and low executive demand situations. This was interpreted as consistent with the suggestion that the difficulties of people with RRMS on complex cognitive tasks are not attributable to a specific decrement in the aspects of executive functioning measured by the Hotel Task, including planning and switching abilities. One exception to this was prospective memory, which was found to be significantly impaired in people with RRMS, consistent with previous studies. This ability may warrant further research in people with MS. Findings on traditional neuropsychological tasks demonstrated results consistent with previous literature, including difficulties with processing speed, delayed verbal memory and some types of executive functioning, although some of these difficulties may be in part explained by slowed information processing.

Suggestions for future areas of research were proposed in order to account for some of the limitations of the current study, as well as to further explore executive functioning, prospective memory and ecological validity of tasks in relation to MS. In particular, it would be useful to replicate the findings of the current study in a larger sample size, including depressed and non-depressed

groups, with an improved Hotel Task. This study has some clear implications for the assessment and management of MS, particularly in relation to difficulties in everyday functioning. One major implication relates to the importance of the assessment and rehabilitation of prospective memory in RRMS.

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Appendices

Appendix 1: Confirmation of Ethical Opinion Letter

NHS
Health Research Authority
NRES Committee London - Dulwich
Health Research Authority
Skipton House
80 London Road
London
SE1 6LH

Telephone: 020 7972 2582

15 November 2012

Mr Kevin M Tierney
Clinical Psychologist in Training
King's College London
3rd Floor, ASB
4 Windsor Walk
Denmark Hill
London SE5 8AF

Dear Mr Tierney

Study title:	**An investigation of cognitive impairments in Relapsing Remitting Multiple Sclerosis using an ecologically valid test of executive functioning**
REC reference:	**12/LO/1306**
Protocol number:	**CSA/12/013**

Thank you for your letter of 12 October 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter	Response to unfavourable opinion letter	20 July 2012
Evidence of insurance or indemnity		02 August 2011
GP/Consultant Information Sheets		
Interview Schedules/Topic Guides	Employment questions v: 1.1	11 May 2012
Interview Schedules/Topic Guides	Guy's Neurological Disability Scale - Lower Limb disability	
Investigator CV		14 May 2012
Letter of invitation to participant	1.1	16 July 2012
Other: Informant invitation letter	1.1	20 July 2012
Other: Unfavourable Opinion Letter		27 June 2012
Participant Consent Form: Informant	2.2	12 October 2012
Participant Consent Form: MS Group	2.2	12 October 2012
Participant Consent Form: Healthy Control	2.2	12 October 2012
Participant Information Sheet: Healthy Control	2.2	12 October 2012
Participant Information Sheet: MS Group	2.2	12 October 2012
Participant Information Sheet: Informant	2.2	12 October 2012
Protocol	2	23 July 2012
Questionnaire: National Adult reading test		
Questionnaire: Montreal Cognitive Assessment		
Questionnaire: Symbol digits Modality task		
Questionnaire: Logical Memory		
Questionnaire: Digit span		
Questionnaire: Hayling task		

Questionnaire: Controlled oral word association test (COWAT)		
Questionnaire: Trail making task		
Questionnaire: Modified fatigue impact scale (MFIS)		
Questionnaire: Centre for epidemiological studies - depression scale (CES-D)		
Questionnaire: Frontal Systems behaviour scale (FrSBE) - Family Rating Form		
Questionnaire: Instrumental activites of daily life (IADL)		
Questionnaire: Hotel task: standard & structured version instructions		
REC application		23 July 2012
Referees or other scientific critique report		12 July 2012
Response to Request for Further Information		12 October 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/LO/1306	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

pp

Dr Michael Philpot
Chair

Email: nrescommittee.london-dulwich@nhs.net

Enclosures: "After ethical review – guidance for researchers" *SL-AR2*

Copy to: *Ms Jenny Liebscher*
Ms Sharan Sandhu, South London Healthcare NHS Trust

Appendix 2: Participant Information Pack (Participants with MS)

King's College Hospital
Neurology Department
Denmark Hill
London
SE5 9RS

16 July 2012

Hello,

Re: Invitation to take part in research on thinking abilities and Multiple Sclerosis

You are attending my Multiple Sclerosis Clinic for neurological appointments. This letter is to invite you to also take part in some research that we are conducting alongside some researchers from King's College London. I am contacting you as I feel you would be suitable to take part in this research.

You do not have to take part in this research. The clinical care you receive will not be affected in any way by the decision you make.

Please find enclosed some information sheets on the research.

- The *Participant Information Sheet* is for you to read and explains what the research is about and what would happen if you take part.
- The *Family Member Information Sheet* is for someone who knows you well, such as your partner or a family member. If you are interested in taking part, your family member will be asked to complete two questionnaires only, and so they do not have to attend your next appointment with you.

If you are interested in taking part in research, please read through the information sheets before your next clinical appointment and consider whether you would be interested in taking part in this particular project.

On the day of your next clinical appointment, I or one of my colleagues will ask if you would be interested in discussing the research with a researcher, who will be able to answer any questions you have.

If you agree to take part in the research, the research session will be carried out at the time that suits you best on the day of your clinic appointment, or at another convenient time.

Thank you for taking the time to read through this letter. I look forward to seeing you at your next appointment.

Yours Sincerely,

Dr. Eli Silber
Consultant Neurologist

South London Healthcare NHS
NHS Trust

Institute of Psychiatry at The Maudsley

KING'S College LONDON

Kevin Tierney
PO78, Department of Psychology
Institute of Psychiatry
London SE5 8AF
Tel: 020 7848 0733
Email: kevin.tierney@kcl.ac.uk

Participant Information Sheet

Version 2.2 – 12.10.2012

Study Title: Assessing Subtle Cognitive Difficulties in Multiple Sclerosis
(Research Ethics Committee Ref: 12/LO/1306; Protocol version 2.0)

Invitation

We would like to invite you to take part in a research study. **If you decide not to take part in the research this will not affect the standard of care you receive in any way.** Before you decide we would like you to understand why the research is being done and what it would involve for you. If you are interested in taking part, one of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes.

The study is being run by Kevin Tierney, Clinical Psychologist in Training, alongside Professor Robin Morris at *King's College London*, as well as Dr Elaine German and Dr Eli Silber at *King's College Hospital NHS Foundation Trust*. The study is an educational project, being carried out as part of a Doctorate in Clinical Psychology at the Institute of Psychiatry. The study forms part of ongoing research into multiple sclerosis, conducted by Professor Robin Morris, Dr Eli Silver and Dr Elaine German.

There are two sections: **Part 1** tells you the purpose of the study and what will happen if you take part. **Part 2** gives you more detailed information about the conduct of the study

Talk to others about the study if you wish. Ask us if anything is not clear.

Part 1: Study Information

What is the purpose of the study?
The study will use tasks that are designed to detect problems with everyday abilities, such as multitasking and planning. These are often the types of difficulties which affect our everyday lives. This study will compare a more 'real world' assessment of these abilities with conventional assessments of difficulties in multiple sclerosis. There are almost no previous research studies that have used these 'real world' assessments with people with multiple sclerosis currently, and so we think it is important to carry out more research on these.

Why have I been invited?
You were chosen because of your condition (multiple sclerosis). You were identified by members of the clinical team at the place where you receive care. The study will aim to recruit approximately thirty people with multiple sclerosis and approximately thirty people without any major medical condition.

Do I have to take part?
It is up to you to decide if you want to take part. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. **You are free to withdraw at any time, without giving a reason. A decision to not take part in the study (or to withdraw from the study) will not affect the standard of care you receive.**

What will happen to me if I take part?
The researcher will see you in order to carry out the research session. If convenient, this will take place on the day of your clinical appointment at the MS Clinic. Otherwise, the researcher will arrange to see you at another time to carry out the research session.

- If you choose to carry out the research on the day of your clinical appointment, **your appointment will always take priority over the research session.** The research session will be arranged either before or after your clinical appointment, as is convenient for you, to ensure that your appointment is not affected.
- If you choose to return to the hospital on a different day to take part in the research, your travel expenses for your journey to the hospital will be refunded.

During the research session, the study will be explained, there will be a short interview and you will be asked to complete a number of tasks, each lasting between one minute and twenty minutes. Overall, the

research session will last up to 2 hours on a single day. This will include time for breaks, so that you can have a rest during the session. The research session is a one off meeting with the researcher and you will not be asked to meet with the researcher again.

You will also be asked to complete some questionnaires at home, which you can return by post. These should take on average 10 minutes to complete. We will provide support over the phone if you would like this. You will receive £10 for your participation in this research.

We would also like to ask your partner, family member or someone close to you to complete two brief questionnaires. These questionnaires will be similar to the ones you will fill out. We will ask you to provide us with the name of someone who knows you well. These questionnaires are to get another view on some of the difficulties you might be having in daily life. Any information given on these questionnaires is confidential.

What are the possible disadvantages and risk of taking part?
There are no major risks or disadvantages to taking part. The research will take about up to 2 hours including time for breaks. You may experience some fatigue whilst doing the research. **Taking part will not affect the care you currently receive.**

What are the possible benefits of taking part?
We do not think that the study will help you directly but the information we get from this study will help improve our understanding of multiple sclerosis and our ability to identify problems people with multiple sclerosis experience.

Will my taking part in this study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2: Detailed Information on Conducting the Study

What will happen if I don't want to carry on with the study?
If you withdraw from the study at any time, this will not affect the clinical care you receive. We may use the data collected up to the point at which you withdraw if you agree to this.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Kevin Tierney, 020 7848 0733). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedures. Details can be obtained through Queen Elizabeth Hospital (telephone: 020 8836 4592 or email: complaints.qeht@nhs.net).

Will my taking part in this study be kept confidential?
All the information collected for the study will be kept strictly confidential, and any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised. Your name and personal details will be kept separately to any other information you give us and will be identified only with a code number. Your information will never be made available to current or future employers. The information provided by your partner or family member will also be kept confidential.

What will happen to the results of the research study?
If you have any concerns about how multiple sclerosis may have affected your thinking skills, please contact your Consultant Neurologist, or ask us to contact them on your behalf. If you would like us to pass on the results of the research assessments you completed to your Consultant Neurologist, we would be happy to do so. Your neurologist or another member of your usual clinical care team will then discuss any concerns with you.

Once the research is completed, you will receive a summary explaining our findings if you choose for this to happen. This summary will describe how the groups of people performed, but it will not include information about your own performance. The results of the research will be published in scientific journals and may be presented to other professionals.

Who is organizing and funding the research?

This study is being organised by the research team (Kevin Tierney, Professor Robin Morris, Dr Elaine German, Dr Eli Silber). King's College London will pay for including you in this study.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and approved by London-Dulwich Research Ethics Committee.

Contact for Further Information

Researcher:	Kevin Tierney (Clinical Psychologist in Training)
Telephone:	020 7848 0733
Address:	Department of Psychology, PO Box 78, Institute of Psychiatry, London SE5 8AF

You will be given a copy of this information sheet and a signed consent from to keep.

South London Healthcare NHS
NHS Trust
Institute of Psychiatry at The Maudsley
KING'S College LONDON

Kevin Tierney
PO78, Department of Psychology
Institute of Psychiatry
London SE5 8AF
Tel: 020 7848 0733
Email: kevin.tierney@kcl.ac.uk

Family Member Information Sheet

Version 2.2 – 12.10.2012

Study Title: Assessing Subtle Cognitive Difficulties in Multiple Sclerosis
(Research Ethics Committee Ref: 12/LO/1306; Protocol version 2.0)

Invitation

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you over the phone if you have any questions. We'd suggest this should take about 5 minutes.

The study is being run by Kevin Tierney, Clinical Psychologist in Training, alongside Professor Robin Morris at *King's College London*, as well as Dr Elaine German and Dr Eli Silber at *King's College Hospital NHS Foundation Trust*. The study is an educational project, being carried out as part of a Doctorate in Clinical Psychology at the Institute of Psychiatry. The study forms part of ongoing research into multiple sclerosis, conducted by Professor Robin Morris, Dr Eli Silver and Dr Elaine German.

Talk to others about the study if you wish. Ask us if anything is not clear.

What is the purpose of the study?

The study will use tasks that are designed to detect problems with everyday abilities, such as multitasking and planning. These are often the types of difficulties which affect our everyday lives. This study will compare a more 'real world' assessment of these abilities with conventional assessments of difficulties in multiple sclerosis. There are almost no previous research studies that have used these 'real world' assessments with people with multiple sclerosis currently, and so we think it is important to carry out more research on these.

Why have I been invited?
You were chosen because your partner/family member has a diagnosis of multiple sclerosis (MS). Your family member was identified by members of the clinical team at the place where they receive care, and they named you as someone who knows them well. The study will aim to recruit approximately thirty people with multiple sclerosis and approximately thirty people without any major medical condition.

Do I have to take part?
It is up to you to decide if you want to take part. We will describe the study and go through this information sheet (over the telephone or in person) if you indicate you are interested in taking part. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. A decision to not take part in the study (or to withdraw from the study) will not affect the standard of care you or your partner/family member receives.

What will happen to me if I take part?
If you are interested in taking part, and have any questions or would like to discuss the research, please contact the researcher. If you decide to take part, you will be requested to complete two questionnaires which you will receive in the post. They ask questions about possible difficulties your partner/family member with MS may experience. The information you provide will be kept confidential and will not be shared with anyone outside the research team. Overall, completing these questionnaires should take on average 8 minutes. There is no ongoing involvement in the research. You will receive £5 after taking part in the research study.

What are the possible disadvantages and risk of taking part?
There are no major risks or disadvantages to taking part. Taking part will not affect the care your partner/family member currently receives.

What are the possible benefits of taking part?
We do not think that the study will help you or your partner/family member directly but the information we get from this study will help improve our understanding of multiple sclerosis.

Will my taking part in this study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. All the information collected for the study will be kept strictly confidential, and any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised. Your name and personal details will be

kept separately to any other information you give us and will be identified only with a code number.

What will happen if I don't want to carry on with the study?
If you withdraw from the study at any time, this will not affect the clinical care your partner/family member receives. We may use the data collected up to the point at which you withdraw if you agree to this.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Kevin Tierney, 020 7848 0733). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedures. Details can be obtained through Queen Elizabeth Hospital, Woolwich (telephone: 020 8836 4592 or email: complaints.qeht@nhs.net).

What will happen to the results of the research study?
Once the research is completed, you will receive a summary explaining our findings if you choose for this to happen. Your family member with MS will also be given the option to receive this summary. This summary will describe how the groups of people performed, but it will not include information about the performance of individual people who took part. The results of the research will be published in scientific journals and may be presented to other professionals.

Who is organizing and funding the research?
This study is being organised by the research team (Kevin Tierney, Professor Robin Morris, Dr Elaine German, Dr Eli Silber). King's College London will pay for including you in this study.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and approved by London-Dulwich Research Ethics Committee.

Contact for Further Information

Researcher: Kevin Tierney (Clinical Psychologist in Training)
Telephone: 020 7848 0733
Address: Department of Psychology, PO Box 78,
Institute of Psychiatry, London SE5 8AF

Appendix 3: Participant Information Sheet (Healthy Control Participants)

South London Healthcare NHS

NHS Trust

Institute of Psychiatry at The Maudsley

KING'S College LONDON

Kevin Tierney
PO78, Department of Psychology
Institute of Psychiatry
London SE5 8AF
Tel: 020 7848 0733
Email: kevin.tierney@kcl.ac.uk

Participant Information Sheet

Version 2.2 – 12.10.2012

Study Title: Assessing Subtle Cognitive Difficulties in Multiple Sclerosis
(Research Ethics Committee Ref: 12/LO/1306; Protocol version 2.0)

Invitation

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes.

The study is being run by Kevin Tierney, Clinical Psychologist in Training, alongside Professor Robin Morris at *King's College London*, as well as Dr Elaine German and Dr Eli Silber at *King's College Hospital NHS Foundation Trust*. The study is an educational project, being carried out as part of a Doctorate in Clinical Psychology at the Institute of Psychiatry. The study forms part of ongoing research into multiple sclerosis, conducted by Professor Robin Morris, Dr Eli Silver and Dr Elaine German.

There are two sections: **Part 1** tells you the purpose of the study and what will happen if you take part. **Part 2** gives you more detailed information about the conduct of the study

Talk to others about the study if you wish. Ask us if anything is not clear.

Part 1: Study Information

What is the purpose of the study?
The study will use tasks that are designed to detect problems with everyday abilities, such as multitasking and planning. These are often the types of difficulties which affect our everyday lives and the ability to continue working. This study will compare a more 'real world' assessment of these abilities with conventional assessments of difficulties in multiple sclerosis. There are almost no previous research studies that have used these 'real world' assessments with people with multiple sclerosis currently, and so we think it is important to carry out more research on these.

Why have I been invited?
You were chosen as a potential participant in the healthy control group. The participation of healthy adults like you is very important to our project, as it provides comparison values for the information we will get from the people with multiple sclerosis.

Do I have to take part?
It is up to you to decide if you want to take part. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. **You are free to withdraw at any time, without giving a reason, and this will have no consequences for you.**

What will happen to me if I take part?
The researcher who reviews this information sheet with you will see you on one occasion in order to carry out the research session. The study will be explained, there will be a short interview and you will be asked to complete a number of cognitive tasks, which last between one minute and twenty minutes. Overall, the research session will last up to 2 hours. The interview and cognitive assessment will take approximately 90 minutes to complete, in addition to time for breaks. You will also be asked to complete three questionnaires which should take on average 8 minutes. The research session is a one off meeting with the researcher and you will not be asked to meet with the researcher again. You will receive £10 for completing the research study.

What are the possible disadvantages and risk of taking part?
There are no major risks or disadvantages to taking part. Taking part will not affect any care you currently receive.

What are the possible benefits of taking part?

We do not think that the study will help you directly but the information we get from this study will help improve our understanding of multiple sclerosis.

Will my taking part in this study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2: Detailed Information on Conducting the Study

What will happen if I don't want to carry on with the study?
If you withdraw from the study at any time, this will not affect the clinical care you receive. We may use the data collected up to the point at which you withdraw if you agree to this.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Kevin Tierney, 020 7848 0733). If you remain unhappy and wish to complain formally, you can do this through King's College London Complaints Procedures. Details can be obtained through King's College London Research Ethics Office (rec@kcl.ac.uk).

Will my taking part in this study be kept confidential?
All the information collected for the study will be kept strictly confidential, and any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised. Your name and personal details will be kept separately to any other information you give us and will be identified only with a code number.

What will happen to the results of the research study?
Once the research is completed, you will receive a summary explaining our findings if you choose for this to happen. This summary will describe how the groups of people performed, rather than giving you information about your own performance. The results of the research will be published in scientific journals and may be presented to other professionals.

Who is organizing and funding the research?
This study is being organised by the research team (Kevin Tierney, Professor Robin Morris, Dr Elaine German, Dr Eli Silber). King's College London will pay for including you in this study.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and approved by London-Dulwich Research Ethics Committee.

Contact for Further Information

Researcher: Kevin Tierney (Clinical Psychologist in Training)
Telephone: 020 7848 0733
Address: Department of Psychology, PO Box 78,
Institute of Psychiatry, London SE5 8AF

You will be given a copy of this information sheet and a signed consent from to keep.

Appendix 4: Verbal Task Instructions for the Hotel Task: Standard Condition

Say to participant:

"*In this task you are asked to imagine that you are working in a hotel. Your manager is keen for you to try each of these six everyday activities during the next 15 min so that you can get a 'feel' for the work—and make an informed estimate of how long each would take to complete. Your main job is therefore to try to do at least some of all these six tasks over the next 15 min. There are six main tasks to do. Each of the tasks may well take longer than 15 min to complete on its own so there is no way that you will be able to complete them all. The most important thing is to try and do something from each task—spending as much time on each as possible within the total time available.*"

Then:
Describe the details of each task and use the materials to demonstrate the task to the participant. After each description, and to avoid omissions due to poor memory for the instructions, a written summary of the task should be placed on top of the relevant materials.

Compiling individual bills
"*This till roll shows which hotel services were used by which guest, and their cost. There is a bill for each individual guest, please write down a list of each service used by a guest on their bill.*"

Sorting the charity collection
"*Please sort these coins into bags containing exactly £1.00 each. Only British currency can be accepted.*"

Sorting cards for the Hotel casino
"*Several packs of playing cards have been mixed up, the casino needs them to be sorted into single packs and into the correct order.*"

Sorting conference labels
"*Please sort these name tags into alphabetical order based on each guest's surname.*"

Proofreading the hotel leaflet
"*Please read the leaflet carefully and cross out any typing mistakes you can find.*"

Opening and Closing the delivery doors
"*A delivery is arriving at the hotel soon. Please open the garage door at 11:06 and close it again 11:12.*"

Then:

- Ask the participant to explain each task to you, and summarise his/her main goal. Only continue if s/he understands the main goal - to try and do as much as possible from each of the tasks within the 15 min available.
- Show participant the clock. Explain that the task will start at "11 o'clock" and run until fifteen minutes past. Say that the clock will be covered, but that they can check the clock whenever they want, the cover is just so that the researcher can see when the participant does this. Set the time to 11 o'clock. Start your stopwatch at the same time.
- Note down the time at which activity started and stopped, and the times at which the clock was consulted.
- If after 5 min of the task, a participant is still engaged in the first task attempted, s/he is to be given a reminder of the primary aim of completing something from each task. No further prompts should be given.
- After 15 minutes ask the participant to stop. Then ask them to again describe briefly what they had to do in each task and their overall aims during the session.

Appendix 5: Verbal Task Instructions for the Hotel Task: Structured Condition

"*Earlier I asked you carry out some tasks that you might carry out if you are working in a hotel. I would now like you to complete these tasks again, following the same instructions, however this time I will give you some suggestions and advice about how to get as much done as possible in the time you have.*

As a reminder, your main job is to try and do at least some of all these six tasks over the next 15 minutes. There are six main tasks to do, and each of these tasks may well take longer than 15 minutes to complete on its own, so there's no way that you will be able to complete them all. The most important thing is to try and do something from each task—spending as much time on each as possible within the total time available.

Here is the recommended plan. Basically, it gives you three minutes for each of the five ongoing tasks, and reminds you to open and close the garage doors at the correct times. I will remind you when it is time to move onto the next task on the list."

Then:
Briefly go through the individual tasks again, placing the written summary on top of the materials. Give the participant a sheet with the recommended structure

Then

- Ask the participant to explain the main task. Only continue if s/he understands the main goal - to try and do as much as possible from each of the tasks within the 15 min available.
- Set the time to 11 o'clock. Start your stopwatch at the same time.
- Note down the time at which activity started and stopped, and the times at which the clock was consulted.
- Remind the participant to move onto the next task on the list every 3 minutes.
- After 15 minutes ask the participant to stop. Then ask them to again describe briefly what they had to do in each task and their overall aims during the session.

Appendix 6: Hotel Task: Structured Condition "Recommended Plan"

Hotel Task – Recommended Plan

We recommend the following structure when completing the 6 tasks:

Task	Time
1) Compiling Individual Bills	11:00 – 11:03
2) Sorting the Charity Collection	11:03 – 11:06
3) Open the Garage Door	11.06
4) Find the phone numbers	11:06 – 11:09
5) Sorting Conference Labels	11:09 – 11:12
6) Close the Garage Door	11.12
7) Proofreading the Hotel Leaflet	11:12 – 11:15

I will remind you when it is time to carry out a task or to change tasks.

Appendix 7: Background Information and Inclusion Screening Record Form

Participant ID		Date	
Gender		Age	
Ethnicity		MS Onset	

Background Information

Years of education:						
Current Employment Status:						
Current / Previous Career						
GNDS-LL Score:	0	1	2	3	4	5
MoCA Score:						

Has the person undergone any previous cognitive assessment? YES NO

Was this within the last 12 months? YES NO

Check Inclusion Criteria:

Diagnosis of Relapsing remitting MS YES NO

Age 18-65 YES NO

Check Exclusion Criteria

Diagnosis in last 12 months YES NO

Relapse in MS over last 4 weeks YES NO

Severe cognitive impairment YES NO

Medical condition affecting cognition YES NO

Major psychiatric illness YES NO

Major substance misuse YES NO

Fatigue/Disability -> interferes w/Ax YES NO

Non-fluent English YES NO

Other Information:

Handedness: Right / Left

Visual impairment Yes / No Corrected: Yes / No

Motor impairment Yes / No Impact on Ax: Yes / No

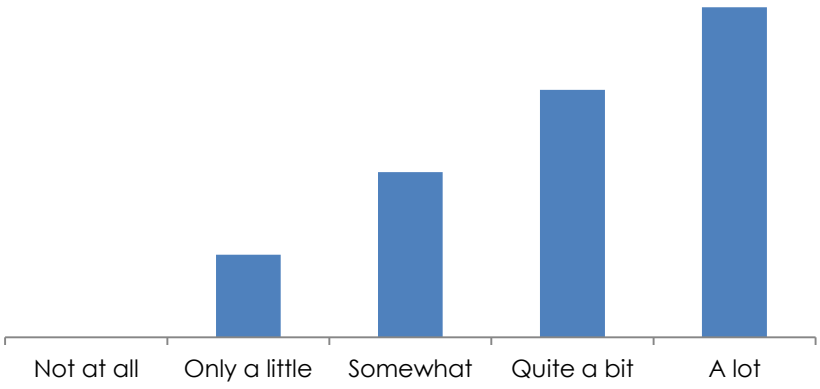
Is this participant eligible for the study? YES / NO

Appendix 8: Employment Questions Record Form

Employment Questionnaire

		Please circle:	
Are you currently employed?		Yes	No
If NO:			
When did you become unemployed?			
Do you have other responsibilities (eg. Managing a household, full time parent, etc)		Yes	No
If so, how would you describe this?			
Details of highest previous employment			
If YES:			
What is your job?			
Is this a paid role?		Yes	No
How many hours per week do you work?			

	Not at all	Only a little	Somewhat	Quite a bit	A lot
Overall, how much has multiple sclerosis impacted on your work?	0	1	2	3	4
How much has each of the following impacted on your work:					
Physical and Neurological Symptoms (e.g. difficulty walking, headaches)	0	1	2	3	4
Fatigue and tiredness	0	1	2	3	4
Cognitive Impairments (e.g. problems concentrating, disorganisation, forgetting etc)	0	1	2	3	4



Appendix 9: Summary of the classifications described in the Standard Occupational Classification 2010 (SOC2010 UK)

Major group	General nature of qualifications, training and experience for occupations in the major group
Managers, directors and senior officials	A significant amount of knowledge and experience of the production processes and service requirements associated with the efficient functioning of organisations and businesses
Professional occupations	A degree or equivalent qualification, with some occupations requiring postgraduate qualifications and/or a formal period of experience-related training.
Associate professional and technical occupations	An associated high-level vocational qualification, often involving a substantial period of full-time training or further study. Some additional task-related training is usually provided through a formal period of induction.
Administrative and secretarial occupations	A good standard of general education. Certain occupations will require further additional vocational training to a well-defined standard (e.g. office skills).
Skilled trades occupations	A substantial period of training, often provided by means of a work based training programme.
Caring, leisure and other service occupations	A good standard of general education. Certain occupations will require further additional vocational training, often provided by means of a work-based training programme.
Sales and customer service occupations	A general education and a programme of work-based training related to Sales procedures. Some occupations require additional specific technical knowledge but are included in this major group because the primary task involves selling.
Process, plant and machine operatives	The knowledge and experience necessary to operate vehicles and other mobile and stationary machinery, to operate and monitor industrial plant and equipment, to assemble products from component parts according to strict rules and procedures and subject assembled parts to routine tests. Most occupations in this major group will specify a minimum standard of competence for associated tasks and will have a related period of formal training.
Elementary occupations	Occupations classified at this level will usually require a minimum general level of education (that is, that which is acquired by the end of the period of compulsory education). Some occupations at this level will also have short periods of work-related training in areas such as health and safety, food hygiene, and customer service requirements.

Appendix 10: Guy's Neurological Disability Scale – Lower Limb disability (GNDS-LL)

The Guy's Neurological Disability Scale (Sharrack & Huges, 1999)

Lower limb disability:

A. Interview

Do you have any problems with your walking?

□ Yes □ No

If 'yes':

Do you use a walking aid?

□ Yes □ No

If 'yes':

A. How do you *usually* get around outdoors?

□ without aid

Or □ with one stick or crutch OR holding on o someone's arm

Or □ with two sticks or crutches OR one stick or crutch and holding on to someone's arm

Or □ with a wheelchair

B. How do you *usually* get around indoors?

□ without aid

Or □ with one stick or crutch OR holding on o someone's arm

Or □ with two sticks or crutches OR one stick or crutch and holding on to someone's arm

Or □ with a wheelchair

If you use a wheelchair:

Can you stand or walk a few steps with help?

□ Yes □ No

B. Scoring

0 - Walking is not affected

1 - Walking is affected but patient is able to walk independently

2 - Usually uses unilateral support (single stick or crutch, one arm) to walk outdoors, but walks independently indoors

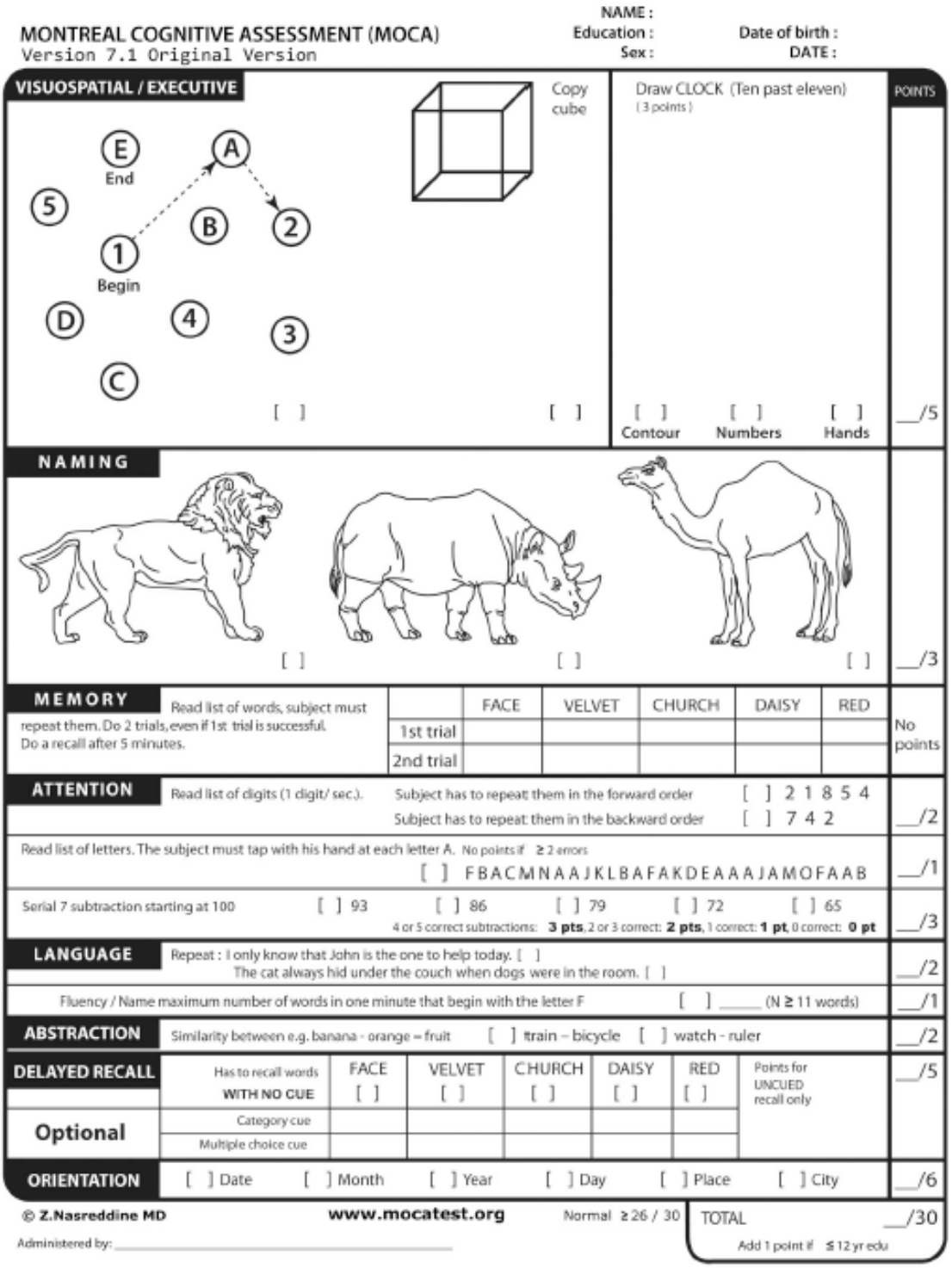
3 - Usually uses bilateral support (two sticks or crutches, frame, or two arms) to walk outdoors, or unilateral support (single stick or crutch, or one arm) to walk indoors

4 - Usually uses wheelchair to travel outdoors, or bilateral support (two sticks or crutches, frame or two arms) to walk indoors

5 - Usually uses a wheelchair indoors

From Sharrack & Hughes (1999). Multiple Sclerosis, 5, 223-233.

Appendix 11: Montreal Cognitive Assessment (MoCA)



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE — POINTS

Copy cube [ ]

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C [ ]

Draw CLOCK (Ten past eleven) (3 points) [ ] Contour [ ] Numbers [ ] Hands /5

NAMING [ ] [ ] [ ] /3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2 /2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B /1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** /3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] /2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) /1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler /2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City /6

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL /30
Add 1 point if ≤ 12 yr edu

Administered by: _____

Appendix 12: Modified Fatigue Impact Scale (MFIS)

Modified Fatigue Impact Scale (MFIS)

Following is a list of statements that describe how fatigue may affect a person. Fatigue is a feeling of physical tiredness and lack of energy that many people experience from time to time. In medical conditions like MS, feelings of fatigue can occur more often and have a greater impact than usual.

Please read each statement carefully, and then **circle the one number** that best indicates how often fatigue has affected you in this way during the **past 4 weeks**. **Please answer every question**. If you are not sure which answer to select, please choose the one answer that comes closest to describing you.

Because of my fatigue, during the past 4 weeks....	**Never**	**Rarely**	**Some-times**	**Often**	**Almost Always**
1 I have been less alert	0	1	2	3	4
2 I have had difficulty paying attention for long periods of time	0	1	2	3	4
3 I have been unable to think clearly	0	1	2	3	4
4 I have been clumsy and uncoordinated	0	1	2	3	4
5 I have been forgetful	0	1	2	3	4
6 I have had to pace myself in physical activities	0	1	2	3	4
7 I have been less motivated to do anything that requires physical effort	0	1	2	3	4
8 I have been less motivated to participate in social activities	0	1	2	3	4
9 I have been limited in my ability to do things away from home	0	1	2	3	4
10 I have had trouble maintaining physical effort for long periods	0	1	2	3	4
11 I have had difficulty making decisions	0	1	2	3	4
12 I have been less motivated to do anything that requires thinking	0	1	2	3	4
13 My muscles have felt weak	0	1	2	3	4

14	I have been physically uncomfortable	0	1	2	3	4
15	I have had trouble finishing tasks that require thinking	0	1	2	3	4
16	I have had difficulty organising my thoughts when doing things at home or at work	0	1	2	3	4
17	I have been less able to complete tasks that require physical effort	0	1	2	3	4
18	My thinking has been slowed down	0	1	2	3	4
19	I have had trouble concentrating	0	1	2	3	4
20	I have limited my physical activities	0	1	2	3	4
21	I have needed to rest more often or for longer periods	0	1	2	3	4

Appendix13: Centre for Epidemiological Studies – Depression Scale (CES-D)

Centre for Epidemiological Studies – Depression Scale

Please circle the number of each statement which best describes how often you felt or behaved this way **during the past week**.

		Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of the time (3-4 days)	Most or all of the time (5-7 days)
1	I was bothered by things that didn't usually bother me	0	1	2	3
2	I did not feel like eating; my appetite was poor	0	1	2	3
3	I felt that I could not shake off the blues even with help from my family and friends	0	1	2	3
4	I felt that I was just as good as other people	0	1	2	3
5	I had trouble keeping my mind on what I was doing	0	1	2	3
6	I felt depressed	0	1	2	3
7	I felt that everything I did was an effort	0	1	2	3
8	I felt hopeful about the future	0	1	2	3
9	I thought my life had been a failure	0	1	2	3
10	I felt fearful	0	1	2	3
11	My sleep was restless	0	1	2	3
12	I as happy	0	1	2	3
13	I talked less than usual	0	1	2	3

14	I felt lonely	0	1	2	3
15	People were unfriendly	0	1	2	3
16	I enjoyed life	0	1	2	3
17	I had crying spells	0	1	2	3
18	I felt sad	0	1	2	3
19	I felt that people disliked me	0	1	2	3
20	I could not get 'going'	0	1	2	3

Appendix 14: Instrumental Activities of Daily Living scale (IADL)

Instrumental Activities of Daily Living

This questionnaire describes everyday activities that people can have difficulty with.

There are eight categories. For each category, **please underline** the statement which best describes your partner/family member's functioning at the moment.

"*Not applicable*" should be underlined if there is no opportunity for the activity, or if your partner/family member typically does this activity less than once a month.

A	Ability to use the telephone
1	She can operate the telephone on her own initiative (e.g. look up and dial numbers)
2	She can dial a few well known numbers
3	She can answer the telephone but does not dial numbers
4	She does not use the telephone at all
9	*(Not applicable)*

B	Shopping
1	She takes care of all her shopping needs independently
2	She shops independently for small purchases
3	She needs to be accompanied on any shopping trip
4	She is completely unable to shop
9	*(Not applicable)*

C	Food preparation
1	She plans, prepares and serves adequate meals independently

E	Laundry
1	She does personal laundry completely
2	She launders small items (rinses socks, stocking, etc)
3	All her laundry must be done by others
9	*(Not applicable)*

F	Mode of transportation
1	She travels independently on public transport or drives her own car
2	She arranges travel by taxi, but does not otherwise use public transportation
3	She travels on public transportation when accompanied by another
4	Her travel is limited to taxi or automobile with the assistance of another person
5	She does not travel at all
9	*(Not applicable)*

G	Responsibility for own medications
1	She is responsible for taking medication in correct dosages at the correct time

2	She prepares adequate meals if supplied with ingredients	2	She takes responsibility if her medication is prepared in advance in separate dosage.
3	She heats, serves and prepares meals or prepares meals but does not maintain adequate diet.	3	She is not capable of dispensing her own medication
4	She needs to have meals prepared and served for her.	*9*	*(Not applicable)*
9	*(Not applicable)*		

D	**Housekeeping**	**H**	**Ability to Handle Finances**
1	She maintains the house alone or with occasional assistance (e.g. “heavy work domestic help”)	1	She manages her financial matters independently (budgets, writes cheques, pays rent/bills, goes to bank), collects and keeps track of income
2	She performs light daily tasks such as dishwashing, bed making	2	She manages day-to-day purchases, but needs help with banking, major purchases, etc.
3	She needs help with all home maintenance tasks	3	She is incapable of handling money.
4	She does not participate in any housekeeping tasks	*9*	*(Not applicable)*
9	*(Not applicable)*		

Appendix 15: Hotel Task: Summary of Subtask Instructions

Could you sort the money from the charity collection, please?

Some of the coins are foreign, so they need to be separated out first.

Then the English coins need to be sorted into the bank bags, with £1 in each bag.

Could you proof-read the new leaflet for the hotel, please?

The typist keeps typing letters twice, by accident, like this -

neww menu

You need to read through the text and circle any mistakes you find.

Could you sort the conference name labels into alphabetical order, please?

Sort them by surname.

Could you write out the customer bills, please?

The list of charges has all the charges which need to be billed to each customer.

You need to search through the list to find all the charges for each customer, and write them on the bills.

Could you look up this list of local companies in the directory please?

Please write down the full telephone number beside the company name.

Could you open and close the delivery doors at these times, please:

open: 11.06 **close:** 11.12

There are two buttons on the desk. The black one will open the doors and the red one will close them.

You need to press the correct button at the time written on this note.

Appendix 16: Sample of the task materials from Hotel Task: Compiling Bills

List of Charges

Mr. Ford	room service	1.95
Mrs. Battersby	bar bill	2.90
Dr. Henderson	newspapers	3.00
Dr. Henderson	newspapers	3.00
Dr. Pern	newspapers	3.00
Dr. Pern	newspapers	3.00
Mr. Ford	newspapers	3.00
Mr. Ford	newspapers	3.00
Mr. Johannes	newspapers	3.00
Mr. Johannes	newspapers	3.00
Mr. Knight	newspapers	3.00
Mr. Knight	newspapers	3.00
Mr. Robertson	newspapers	3.00
Mr. Robertson	newspapers	3.00
Mr. Tan	newspapers	3.00
Mr. Tan	newspapers	3.00
Mrs. Battersby	newspapers	3.00

The Bay View Hotel

Customer Bill

Customer name: Dr. Pern

List of Charges:

Service: *Cost:*

.....
.....
.....
.....
.....
.....
.....
.....
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Appendix 17: Sample of task materials from Hotel Task: Looking Up Telephone Numbers

Company List

Company	Telephone Number
Hillary's Shutters	
Green Dex Property Maintenance	
Domestic & General	
APS Plumbing Services	
Harradines Removals and Storage	
Westside Electrical Limited	
Cancer Research UK	
Pinnacle Heights Roofing Ltd.	
Maintracts Services	
Autonet Van Insurance	
Parchmore Electronics	
Ruskinbuildingservices.co.uk	
Christmas Tree Farm	
Paterson Heath & Co Ltd.	
Splash Hand Car Wash	
Junction Emporium	
A.B. Key Emergency Locksmith	
Estate Insurance Group	
Chase Legal Services	
S & S Drycleaners	

Appendix 18: Sample of task materials from Hotel Task: Proofreading the Hotel Leaflet

Bay View Hotel, Littleshire, England.

About Bay View

The arrea in which the hotel is set is perhaps one of the most unspoiled - and opulent – in England. Indeed, the locality has become the preferred retreat of the rich & famous, and the hotel perfectly reflects this - a place which very much favours the finer things in life.

Nestled in thirrty acres of rolling countryside, the privately owned Bay View Hotel is a special place of evocative conntrasts offering relaxed luxury and high service standards. Part of Bay View's special appeal is its variety, with abundant leisure activities available, including our adjacent 9-hole golf course, luxurious spa and swimming pool, top-notch cuisine in both of our restaurants, as well as four-star accommodation in a wide range of suites and rooms each with individual quirks and unique charm. We are also able to provide excellent conference facilities suitaable for every corporate event ranging from the informal to the international.

We also offer a range of exciting package deals – spa retreats, adventure breaks and golfing excursions. Therre is further inforrmation on each of these possibilities further on in the brochure, but first why not dedicate a little time to discover the fascinating history behind Bay View Hotel.

The oldest building at Bay Vieww dates back to 1475 and forms part of the rich history of the local area. Cromwell billeted his troops here overnight during the Civil War. In the eighteenth century the building was used as a courthouse and legend suggests that the villains awaited their fate on the bench in the old Auberge de France – one of our restaurants. The property today iss best described as a hamlet of buildings each with its own character. Features around the property enchant and surprise. Antiquities in the old building, a reclaimed church floor in reception, hand painted fabrics and hand crafted furniture are just some of the nottable items that combine to form a fascinating rich tapestry combining the culture and opulence of by-gone days with the comfort and convenience of modern living.

All of the bedrooms have been indivvidually designed and are as memorable for their charm as for their modern convenience. Many offer wonderful views of the surrounding countryside.

Bayy View has two restaurants offering elegant and sophisticated dining in a choice of ancient and modern settings. Intriguing private dining rooms such as *The Pantry* and *The Dungeon* offer something special to contemplate. Whether you are staying for pleasure or on business, the excellent facilities,

the tones and textures, the ambience and hospitality all combine to make your stay a memorable and enjoyable experience.
The spacious ‘Retreat’ Spa follows in the long Bay View tradition of improvement. With its engaging architecture and state-of-the-art spa ffacilities, ‘Retreat’ adds yet more layers of comfort and pleasure to your stay.

Near the Hotel

The hotel is locateed within a designated Area of Outstandding Natural Beauty in a beautiful and peaceful part of the country, a hidden secret, offering a variety of historic attractions and places of interest. The walks to be had along the unbelievably exquisite cliff-tops are a must, as are visits to the numerous gardens along the coast.

In the vicinity of the hotel there is every amenity one could wish for, as well as plenty of visitor attractions. For exxample, there is the famous Portresco Castle, an ancient fortress of great importance during the Spanish Armada, which also boasts fine classical gardens. The open-air theatre productions heere are a splendid way to spend a summer evening, though to err on the side of caution, warm water-resistant clothing is advised to be kept on hand!

For those who enjoy "messinng about in boats", the river and sea are perfect playgrounds. BBoth sailing craft and motor vessels can be hired for the day, allowing for the exploration of numerous coves and creeks. There are also day trips and river tours that can be booked from Bay View reception.

Appendix 19: Consent Forms

South London Healthcare NHS
NHS Trust

Institute of Psychiatry at The Maudsley

KING'S College LONDON

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Institute of Psychiatry
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Tel: 020 7848 0733
Email: kevin.tierney@kcl.ac.uk

Centre Number	
Study Number	
Patient Identification Number	

Participant Consent Form

Version 2.2 – 12.10.2012

Study Title: Assessing Subtle Cognitive Difficulties in Multiple Sclerosis
(Research Ethics Committee Ref: 12/LO/1306; Protocol version 2.0)

Name of the Researcher: Kevin Tierney

		Please tick
1	I have read and understood the information sheet dated 12.10.2012 (version 2.2) for the above study. I have had the opportunity to consider the information and ask questions about the study.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.	
3	I give permission for the researcher and his academic supervisors to have access to my records.	

4 I agree to take part in the above study. ☐

5 I want to receive a letter after the research study has been completed with a summary of the overall research findings. ☐

6 I want my Consultant Neurologist to receive a brief report with a summary of my individual performance on the research tasks and questionnaires that I am about to complete. ☐

Name of Participant	Date	Signature

I have explained the study to the participant and answered their questions honestly and fully.

Name of Researcher	Date	Signature

When completed, 1 copy for participant; 1 copy for central research file; 1 copy to be kept in medical notes

South London Healthcare NHS

NHS Trust

Institute of Psychiatry at The Maudsley

KING'S College LONDON

Kevin Tierney
PO78, Department of Psychology
Institute of Psychiatry
London SE5 8AF
Tel: 020 7848 0733
Email: kevin.tierney@kcl.ac.uk

Centre Number	
Study Number	
Patient Identification Number	

Family Member Consent Form

Version 2.2 – 12.10.2012

Study Title: Assessing Subtle Cognitive Difficulties in Multiple Sclerosis
(Research Ethics Committee Ref: 12/LO/1306; Protocol version 2.0)

Name of the Researcher: Kevin Tierney

		Please tick
1	I have read and understood the information sheet dated 12.10.2012 (version 2.2) for the above study. I have had the opportunity to consider the information and ask questions about the study.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.	
3	I agree to take part in the above study.	
4	I want to receive a letter after the research study has been completed with a summary of the overall research findings.	

Name of Participant	Date	Signature

I have answered any questions honestly and fully.

Name of Researcher	Date	Signature

When completed, 1 copy for participant; 1 copy for central research file

South London Healthcare NHS

NHS Trust

Institute of Psychiatry at The Maudsley

KING'S College LONDON

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Centre Number	
Study Number	
Patient Identification Number	

Control Participant Consent Form

Version 2.2 – 12.10.2012

Study Title: Assessing Subtle Cognitive Difficulties in Multiple Sclerosis
(Research Ethics Committee Ref: 12/LO/1306; Protocol version 2.0)

Name of the Researcher: Kevin Tierney

		Please tick
1	I have read and understood the information sheet dated 12.10.2012 (version 2.2) for the above study. I have had the opportunity to consider the information and ask questions about the study.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.	
3	I agree to take part in the above study.	
4	I want to receive a letter after the research study has been completed with a summary of the overall research findings.	

Name of Participant	Date	Signature

I have explained the study to the participant and answered their questions honestly and fully.

Name of Researcher	Date	Signature

When completed, 1 copy for participant; 1 copy for research site file

Appendix 20: Analysis of Sampling Distribution for Each Dependent Variable

Assessment Measure	Dependent Variable	Assumptions of Normality Met?	Shapiro-Wilk Statistic		Analysis Used
Hotel Task: Standard					
Time Discrepancy	Total Score (z score)	**Yes.**	RRMS: CT:	W(19) = .915, p = .093 W(19) = .957, p = .518	Independent t-test
	Compiling Bills	*No. RRMS data negatively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .862, p = .011** *W(19)= .925, p = .140*	*Independent Samples Mann-Whitney U test*
	Directory Search	No. Normality achieved through Square Root transformation. -> **Yes.**	RRMS: CT:	W(19) = .911, p = .077 W(19) = .937, p = .237	Independent t-test
	Sorting Coins	*No. RRMS data negatively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .848, p = .006** *W (19)= .941, p = .271*	*Independent Samples Mann-Whitney U test*
	Sorting Labels	No. Normality achieved through Square Root transformation. -> **Yes.**	RRMS: CT:	W(19) = .931, p = .181 W(19) = .937, p = .234	Independent t-test
	Proofreading Text	No. Normality achieve through Log (10) transformation. -> **Yes.**	RRMS: CT:	W(19) = .941, p = .280 W(19) = .953, p = .451	Independent t-test
Prospective Memory	*Open Garage Door*	*No. Both groups positively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .507, p = .000** *W(19) = .710, p = .000**	*Independent Samples Mann-Whitney U test*
	Close Garage Door	No. Normality achieved through Log (10) transformation. -> **Yes.**	RRMS: CT:	W(19) = .907, p = .065 W(19) = .915, p = .090	Independent t-test
Tasks Attempted	*Number of Task started*	*No. Little variance in both groups. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .746, p = .000** *W(19) = .651, p = .000**	*Independent Samples Mann-Whitney U test*
Time Monitoring	Number of clock checks	No. Normality achieved through Square Root transformation. -> **Yes.**	RRMS: CT:	W(19) = .933, p = .196 W(19) = .934, p = .202	Independent t-test
Performance Efficiency	Total Score (z score)	**Yes.**	RRMS:	W(19) = .963, p = .630	2 x 2 Mixed Model

			CT:	W(19) = .943, p = .300	ANCOVA
	Compiling Bills	*No. RRMS data positively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .738, p = .000** *W(19) = .906, p = .063*	*Mann-Whitney U test on HTB-HTA difference*
	Directory Search	*No. RRMS data positively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .799, p = .001** *W(19) = .915, p = .090*	*Mann-Whitney U test on HTB-HTA difference*
	Sorting Coins	*No. RRMS data positively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .873, p = .016** *W(19) = .904, p = .058*	*Mann-Whitney U test on HTB-HTA difference*
	Sorting Labels	*No. CT data positively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .962, p = .349* *W(19) = .880, p = .021**	*Mann-Whitney U test on HTB-HTA difference*
	Proofreading Text	**Yes.**	RRMS: CT:	W(19) = .947, p = .349 W(19) = .930, p = .176	*Mann-Whitney U test on HTB-HTA difference*
Hotel Task: Structured					
Performance Efficiency	Total Score (z score)	**Yes.**	RRMS: CT:	W(19) = .973, p = .839 W(19) = .978, p = .915	2 x 2 Mixed Model ANCOVA
	Compiling Bills	**Yes.**	RRMS: CT:	W(19) = .965, p = .669 W(19) = .936, p = .222	*Mann-Whitney U test on HTB-HTA difference*
	Directory Search	*No. Little variance in both groups. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .577, p = .000** *W(19) = .781, p = .001**	*Mann-Whitney U test on HTB-HTA difference*
	Sorting Coins	**Yes.**	RRMS: CT:	W(19) = .977, p = .908 W(19) = .950, p = .393	*Mann-Whitney U test on HTB-HTA difference*
	Sorting Labels	**Yes.**	RRMS: CT:	W(19) = .966, p = .701 W(19) = .956, p = .500	*Mann-Whitney U test on HTB-HTA difference*

	Proofreading Text	**Yes.**	RRMS: CT:	W(19) = .962, p = .609 W(19) = .973, p = .841	*Mann-Whitney U test on HTB-HTA difference*
Background Neuropsychological Assessments					
SDMT	Oral Score	**Yes.**	RRMS: CT:	W(19) = .955, p = .479 W(19) = .961, p = .592	Independent t-test
Verbal Fluency	Letter Fluency	**Yes.**	RRMS: CT:	W(19) = .917, p = .622 W(19) = .961, p = .548	Independent t-test
	Category Fluency	**Yes.**	RRMS: CT:	W(19) = .917, p = .100 W(19) = .961, p = .593	Independent t-test
Logical Memory	LM I: Total	**Yes.**	RRMS: CT:	W(19) = .921, p = .116 W(19) = .957, p = .523	Independent t-test
	LM I: Story A	**Yes.**	RRMS: CT:	W(19) = .965, p = .681 W(19) = .972, p = .809	Independent t-test
	LM I: Story B	**Yes.**	RRMS: CT:	W(19) = .946, p = .332 W(19) = .923, p = .131	Independent t-test
	LM II: Total	**Yes.**	RRMS: CT:	W(19) = .963, p = .627 W(19) = .967, p = .724	Independent t-test
	LM II: Story A	**Yes.**	RRMS: CT:	W(19) = .934, p = .207 W(19) = .930, p = .172	Independent t-test
	LM II: Story B	**Yes.**	RRMS: CT:	W(19) = .974, p = .860 W(19) = .903, p = .055	Independent t-test
	LM Percentage Recall	**Yes.**	RRMS: CT:	W(19) = .969, p = .761 W(19) = .932, p = .188	Independent t-test
Digit Span	DS Total	No. Normality achieved through Log(10) transformation. -> **Yes.**	RRMS: CT:	W(19) = .930, p = .173 W(19) = .904, p = .056	Independent t-test
	DS Forwards	No. Normality achieved through Reciprocal transformation. -> **Yes.**	RRMS: CT:	W(19) = .936, p = .223 W(19) = .908,	Independent t-test

				p = .068	
	DS Backwards	**Yes.**	RRMS: CT:	W(19) = .952, p = .428 W(19) = .934, p = .207	Independent t-test
Hayling Test	*Section 1 Time*	*No. RRMS data positively skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .707, p = .000** *W(19) = .938, p = .244*	*Independent Samples Mann-Whitney U test*
	Section 2 Time	No. Normality achieved through Square Root transformation. -> **Yes.**	RRMS: CT:	W(19) = .979, p = .927 W(19) = .911, p = .076	Independent t-test
	Section 2 Error Score	*No. Little variance in both groups. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .736, p = .000** *W(19) = .552, p = .000**	*Independent Samples Mann-Whitney U test*
Trail Making Test	TMT A Time	No. Normality achieved through Log (10) transformation. -> **Yes.**	RRMS: CT:	W(19) = .964, p = .650 W(19) = .928, p = .161	Independent t-test
	TMT B Time	**Yes.**	RRMS: CT:	W(19) = .941, p = .276 W(19) = 973, p = .837	Independent t-test
	TMT B-A	**Yes.**	RRMS: CT:	W(19) = .969, p = .762 W(19) = .968, p = .734	Independent t-test
NART	Total Errors	No. Normality achieved through Square Root transformation. -> **Yes.**	RRMS: CT:	W(19) = .978, p = .913 W(19) = .935, p = .214	Independent t-test
		Questionnaires			
MFIS	Total Score	**Yes.**	RRMS: CT:	W(18) = .948, p = .401 W(19) = .919, p = .111	Independent t-test
	Physical Subscale	**Yes.**	RRMS: CT:	W(18) = .942, p = .309 W(19) = .912, p = .081	Independent t-test
	Cognitive Subscale	*No. Little Variance in CT data. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(18) = .952, p = .452* *W(18) = .879, p = .020**	*Independent Samples Mann-Whitney U test*
	Psychosocial Subscale	*No. Little Variance in CT data. Not possible to correct by*	*RRMS:* *CT:*	*W(18) = .928, p = .180* *W(19) = .895,*	*Independent Samples Mann-*

		transformation.		*p = .040**	*Whitney U test*
CES-D	Total Score	No. Normality achieved through Square Root transformation. -> **Yes.**	RRMS: CT:	W(18) = .970, p = .801 W(19) = .944, p = .317	Independent t-test
IADL Family Rating	*Total Score*	*No. Little variance in RRMS group.*	*RRMS:*	*W(16) = .775, p = .001**	*Single Group*
FrSBE Self Rating (currently)	Total	**Yes.**	RRMS: CT:	W(18) = .968, p = .757 W(19) = .944, p = .305	Independent t-test, Dependent t-test
	Apathy	**Yes.**	RRMS: CT:	W(18) = .913, p = .096 W(19) = .920, p = .115	Independent t-test, Dependent t-test
	Disinhibition	**Yes.**	RRMS: CT:	W(18) = .908, p = .081 W(19) = .922, p = .124	Independent t-test, Dependent t-test
	Executive Dysfunction	**Yes.**	RRMS: CT:	W(18) = .975, p = .881 W(19) = .918, p = .102	Independent t-test, Dependent t-test
FrSBE Family Rating (currently)	Total	**Yes.**	RRMS:	W(17) = .926, p = .188	Dependent t-test
	Apathy	**Yes.**	RRMS:	W(17) = .935, p = .260	Dependent t-test
	Disinhibition	**Yes.**	RRMS:	W(17) = .948, p = .428	Dependent t-test
	Executive Dysfunction	**Yes.**	RRMS:	W(17) = .921, p = .153	Dependent t-test
FrSBE Self Rating (Prior to MS onset)	Total	**Yes.**	RRMS:	W(17) = .967, p = .773	Dependent t-test
	Apathy	**Yes.**	RRMS:	W(17) = .958, p = .599	Dependent t-test
	Disinhibition	**Yes.**	RRMS:	W(17) = .904, p = .081	Dependent t-test
	Executive Dysfunction	**Yes.**	RRMS:	W(17) = .964, p = .709	Dependent t-test
FrSBE Family Rating (Prior to MS onset)	Total	**Yes.**	RRMS:	W(17) = .974, p = .884	Dependent t-test
	Apathy	**Yes.**	RRMS:	W(17) = .915, p = .124	Dependent t-test
	Disinhibition	**Yes.**	RRMS:	W(17) = .962, p = .679	Dependent t-test
	Executive Dysfunction	**Yes.**	RRMS:	W(17) = .940, p = .322	Dependent t-test
Demographic Variables					
Age	Age (years)	**Yes.**	RRMS: CT:	W(19) = .964, p = .651 W(19) = .931,	Independent t-test

				p = .182	
Education	*Years of Full Time Education*	*No. Both groups' data skewed. Not possible to correct by transformation.*	*RRMS:* *CT:*	*W(19) = .871, p = .015** *W(19) = .879, p = .020**	*Independent Samples Mann-Whitney U test*
NART-R	Estimated FSIQ	No. Normality achieved through Cubing values. -> **Yes.**	RRMS: CT:	W(19) = .976, p = .891 W(19) = .914, p = .160	Independent t-test
MOCA	Total Score	**Yes.**	RRMS: CT:	W(19) = .955, p = .470 W(19) = .923, p = .126	Independent t-test
Working Hours	Working Hours	**Yes.**	RRMS: CT:	W(9) = .954, p = .734 W(10) = .949, p = .656	Independent t-test

Appendix 21: Checking Assumptions for two way mixed model ANOVA

Within Group Difference Scores

Dependent Variable			Statistic	p
Hotel Task Difference Scores	Bills	RRMS	W (19)= .938	.242
		CT	W (19)= .866	**.012**
	Directory	RRMS	W (19)= .951	.411
		CT	W (19)= .958	.536
	Coins	RRMS	W (19)= .987	.993
		CT	W (19)= .917	.099
	Labels	RRMS	W (19)= .854	**.008**
		CT	W (19)= .977	.898
	Proofreading	RRMS	W (19)= .924	.136
		CT	W (19)= .948	.372

Between Group Variance

Dependent Variable		Variance		Variance similar?
		RRMS	Control	
Hotel Task	Bills (A)	1.41	3.60	**No**
	Bills (B)	1.38	2.32	Yes
	Directory (A)	.05	.12	**No**
	Directory (B)	.06	.06	Yes
	Coins (A)	1.04	1.09	Yes
	Coins (B)	.68	.42	Yes
	Labels (A)	9.04	10.03	Yes
	Labels (B)	7.65	12.02	Yes
	Proofreading (A)	4.31	6.18	Yes
	Proofreading (B)	3.06	4.70	Yes

Conclusion

Assumptions violated for 3 out of 5 activities.

Service Evaluation Project

Development, implementation and evaluation of an intervention to improve clinician completion of electronic clinical records in a specialist child and adolescent mental health service

Kevin Tierney
Institute of Psychiatry, King's College London

Supervised by Dr. Daniel Michelson
Discussant: Prof. Derek Bolton

Anxiety and Traumatic Stress Service for Children & Young People
National and Specialist CAMHS

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Abstract

Background

Clinical patient records are an important resource, both at an individual patient level and at an aggregated, corporate level. Inaccurate or incomplete clinical records may put patient safety at risk and facilitate poor clinical practice. Well maintained clinical records can assist appropriate service planning and commissioning. There are a number of policies and organisational systems in place to facilitate good practice in clinical record keeping; however individual decision making has an important role in whether this behaviour is performed. Social cognition theories can be helpful in understanding and changing the behaviour of clinicians.

Aims

This study sought to develop and evaluate an intervention to improve clinician completion of clinical records in CAMHS, drawing on the Theory of Planned Behaviour, previous research and stakeholder perspectives.

Method

Clinical team members were interviewed based on themes identified in the service innovation and implementation literatures. The information gathered in these interviews was used to select intervention components which were feasible and appropriate to the service context, and these were implemented in the service. Impacts of the intervention were evaluated in a comparative pre-post audit of clinical record keeping using standards identified from relevant local trust policies.

Results

A mixed pattern of results showed statistically significant improvements in completion of some fields (C-GAS, Presenting Circumstances, Event Note,

Letter to Referrer) according to the 'Minimum Standard' timescales. Rates of compliance with more stringent 'Best Practice' timescales did not change significantly. Absolute rates of record completion remained below 100%.

Conclusions

A simple and resource-light intervention based on psychological theory can lead to improvements in clinician completion of clinical records. These findings are in line with previous research using social cognition theories to influence changes in professionals' behaviour. However, there remains scope for further improvement in compliance with guidelines on completion of clinical records, and this may be best achieved by directly assessing change in the cognitions and attitudes of clinicians, as well as incorporating interventions which account for the broader organisational context of the service.

1 Introduction

1.1 Clinical Records

1.1.1 An Individual Asset

The Department of Health defines a clinical record as “any paper or electronic-based record which contains information or personal data pertaining to people’s [health] care” (DoH, 2010, p.7). Clinical records are acknowledged as a fundamental aspect of individual patient care within the NHS. Guidelines on clinical record keeping suggest that clinical records can facilitate high quality care for individual service users in five main ways: communication, continuity of care, risk assessment, informed decision making and the rights of service users to access information held about them.

The first main use relates to communication. Clinical records are intended to provide a clear, accurate description of assessments, care plans, clinical events, progress and outcomes. This information can be communicated within and between clinical teams in order to achieve individualised and responsive care (Johnson & Gowers, 2005; Pullen & Loudon, 2006). This information has most value when it is accurate, comprehensive and up-to-date (DoH, 2006).

Relatedly, clinical records support continuity of care through integration of information into a single record. This is particularly important in the context of current changes in society and healthcare provision, in particular the shift from unidisciplinary out-patient clinic and specialist in-patient service to the long-term management of chronic illness (Pullen & Loudon, 2006). Individual clinical records bring together both historical and current information from multiple sources on the service user, including details of problems, context and the care provided.

A third aspect of clinical records is to record any risks identified, and also factors relevant in the service user's engagement in, and response to, treatment.

Fourth, clinical records facilitate effective clinical judgements and the provision of evidence based clinical care in line with best practice guidelines on an individual level via access to detailed information of the difficulty experienced by the service user. Conversely, poor clinical record keeping has a detrimental impact on the care of service users and increases the risk of harm when making decisions or by not appropriately communicating information to relevant parties (NHSLA, 2012). Finally, service users are also entitled to access all records held about them (DoH, 2012) with an associated responsibility that healthcare providers maintain accurate records of the care provided (NIGB, 2011).

1.1.2 A Corporate Asset

Aggregated data from clinical records can also serve a number of important functions at a corporate level. Firstly, clinical records support day-to-day business in the running of healthcare services, such as recording the booking of appointments. They support administrative and clinical decision making, for instance providing information on the attendance rate of a service and waiting list times. In a related point, comprehensive clinical records allow audits to be completed within organisations, be these either clinical or administrative, and thus can contribute to the effective provision and management of services (DoH, 2006).

Secondly, clinical records contribute to improved healthcare at a group level through research and clinical audit. They provide information which may help protect the health of the general public, for example informing public health planning through epidemiological data on the occurrence of various difficulties. They can be used to identify potential participants for clinical

research trials, and can be used to investigate the uptake and acceptability of treatments to service users. A third point relates to training and staff development. Clinical records can also contribute to the teaching of healthcare professionals and can be used to assess the competence of practicing clinicians (NIGB, 2011), as well as to identify training needs of staff based on recorded behaviour.

There is increasingly a move toward increasing service user control and influence over their health and healthcare (e.g. Darzi, 2008). Within this, one goal is to systematically measure and publish information about the quality and performance of healthcare services. Thus a fourth use of clinical records is that they provide a method of capturing this performance data, across diverse domains such as safety, clinical outcome and service satisfaction. Fifth, clinical record keeping also serves financial functions. Information on the number of service users seen by a service, as well as the resources required in a typical intervention can be used to aid costing of future care from a commissioning point of view. Currently there is a plan for 'Payment by Results', a scheme whereby commissioners pay healthcare providers for each service user seen based on the complexity of their needs. Aggregated clinical records may be used in order to estimate care "tariffs" (Audit Commission, 2012).

Finally, clinical records serve legal functions, and may be used as evidence in complaints procedures and negligence claims (NHSLA, 2012). Access is governed by the Data Protection Act, which forms a complex legal framework designed to protect people's privacy by preventing unauthorised or inappropriate use of personal data. This requires that clinical records (both computerised and manual) must be kept in a secure environment with suitable safeguards in place for electronic storage (e.g. password-protected access, encryption and monitoring).

1.2 Theoretical Frameworks for Changing Behaviour

Despite the fundamental importance of clinical records in healthcare provision, there continues to be problems with their completion. For example, the Audit Commission notes that over half of the NHS trusts had at least one case (out of 300) where there was no record of an episode of treatment provided to a service user (Audit Commission, 2010).

Individual NHS employees are legally responsible for the clinical records that they create or use in the course of their duties. These clinical records are also subject to professional obligations. Equally, trusts have a responsibility to have in place policies on the management of records and should provide training on this to members of staff (DoH, 2006). Individual behaviour is important in the implementation of guidelines, and completion of clinical records may remain sub-optimal even when these policies are in place due to lack of change on an individual level. Thus it is useful to draw on social cognitive theories of behaviour change, which consider the cognitive mechanisms underlying behaviour, in order to increase professionals' compliance with these standards (Godin et al., 2008).

One of the most researched theories of behaviour change is the Theory of Planned Behaviour (TPB; Ajzen, 1985; 1987). TPB posits that the likelihood of an individual carrying out a target behaviour is influenced by three factors. First is the individual's attitude to the behaviour, as related to the expected value of performing the behaviour. The second relates to subjective norms, including the individual's perception of what important others think about the behaviour, as well as the individual's motivation to comply with these norms. Finally, the individual's perceived behavioural control influences their behavioural intentions, including self-efficacy around overcoming obstacles to performing the behaviour. For example, when applied to following guidelines in a healthcare setting such as maintaining clinical records, it is important to consider the staff member's views on the expected value of performing this behaviour, their relevant social norms (such as the expectations of their team

and professional body, as well as sources of intrinsic and extrinsic motivation to follow the guidelines) and also to consider how much the staff member feels able to carry out this behaviour.

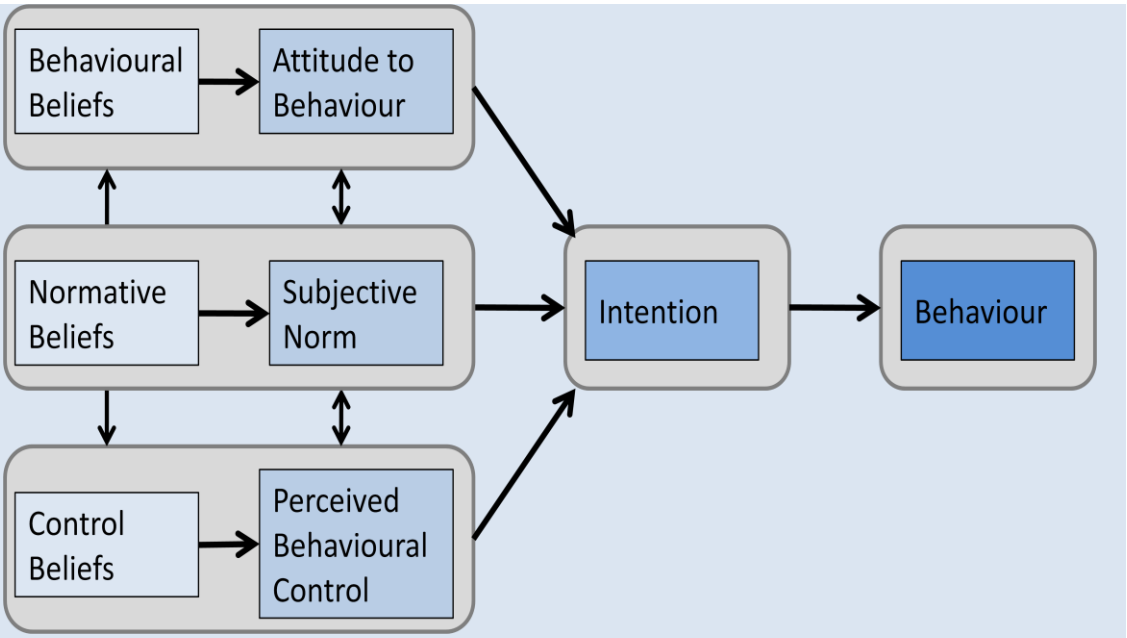

Figure 1: Theory of Planned Behaviour model (Ajzen, 2006).

Applied to individual adoption of new behaviours, this theory predicts that altering the mediators of behaviour intention (attitudes, subjective norms and perceived behavioural control) for individual professionals should lead to a change in their behaviour (Perkins, 2007). A number of additional factors influence the development and change of social cognitions in individual professionals, including organisational context, national and local policies, guidelines from professional bodies, characteristics of the target behaviour as well as individual factors (Greenhalgh et al., 2004). The TPB has most often been used to *explain* behaviour, for instance in understanding doctors' use of clinical guidelines on asthma and antibiotic use (Limbert and Lamb, 2002), and has less commonly been used to detail how to *change* behaviour (Michie et al., 2008).

In terms of individual factors, there have been attempts to draw on the TPB and other relevant theories to develop a comprehensive theoretical approach

towards implementation research, to aid development of interventions to bring about behaviour change. Michie and colleagues (2005) consulted with health psychologists and researchers to develop a theoretical framework with particular utility for understanding implementation of evidence-based practices and behaviour change among healthcare professionals. They identified 12 domains relevant to predicting and changing the behaviour of individual professionals, including knowledge, professional role & identity, motivation & goals, and social influences (Table 1). Many of these domains link in with the TPB, and can be seen as either necessary for performance of a specific behaviour (e.g. strong intention, no environmental constraints, necessary skills) while others can be seen as contributing to the strength of the intention, for instance belief about capabilities and consequences, social influences, emotion (Fishbein et al., 2001).

Table 1: Theoretical domains relevant to behaviour change and examples of constructs within these (adapted from Michie et al., 2005).

Theoretical Domains	Construct examples
1. Knowledge	Knowledge about rationale, procedural knowledge
2. Skills	Competence, skills development
3. Social/professional role and identity	Professional identity, social norms
4. Beliefs about capabilities	Self-efficacy, perceived behavioural control, perceived
5. Beliefs about consequences	Outcome expectancies, attitudes, sanctions/rewards (proximal/distal)
6. Motivation and goals (Intentions)	Stability of intention, goals, goal priority
7. Memory, attention & decision processes	Memory, attention, decision making
8. Environmental context and resources	Material resources, environmental stressors
9. Social Influences (norms)	Social support, social norms, leadership, team working, power/hierarch, social comparison, feedback
10. Emotion	Stress, anxiety, cognitive overload/tiredness
11. Behavioural Regulation	Action planning, self monitoring, moderators of intention-behaviour gap, barriers and facilitators
12. Nature of the Behaviours	Routine/automatic, representation of tasks

1.3 Research on Changing the Behaviour of Health Professionals

Previous reviews of the healthcare implementation literature have concluded that there are no “magic bullets” to change professionals’ behaviour, such that no intervention is effective in all situations and that change is difficult to achieve (Oxman et al., 1995). Instead, interventions need to be sensitively selected based on appropriate understanding of the relevant contextual factors, such as obstacles to performing the behaviour. Multi-faceted interventions, guided by theories of behaviour change, are more likely to result in behaviour change than atheoretical interventions targeting individual domains (Grimshaw et al., 2001; Grimshaw et al., 2004; Grol & Wensing, 2004; Eccles et al., 2012).

Considering professionals’ behaviour specifically, Oxman and colleagues (1995) conducted a systematic review of 102 implementation research studies. Dissemination-only strategies demonstrated little or no change in professionals’ behaviour, while more complex interventions were variable in their effectiveness, but were most often moderately effective. A recent review of one of the most frequently used interventions, printed educational materials, concluded that when used in isolation, these may have a small beneficial effect on the healthcare process, but not necessarily on patient outcomes (Farmer et al., 2009). Other authors have suggested that the quality of interventions is relevant, for example vaguely worded guidelines are less likely to result in behaviour change compared to specific guidelines (Michie & Johnston, 2004).

With regard to intervention research on changing behaviour, Hardeman and colleagues (2005) caution that there is no simple link between theory and choice of intervention techniques, and that selection of interventions to improve professional performance are complex. Eccles and colleagues (2012) compared the ability of several psychological models to predict the behaviour

of health professionals across five studies, and found that the TPB performed best in this regard, although the percentage variance in behaviour accounted for was low overall. Armitage and Conner (2001) carried out a meta-analysis of 185 studies using the TPB to explain behaviour and found that on average the TPB accounted for 39% of the variance in intention and 27% of the variance in actual behaviour.

Nonetheless, there are examples of studies which have successfully targeted clinicians' intentions in order to improve compliance with guidelines. For example, Bonetti and colleagues (2003) assessed the effect of rehearsing alternative behaviour plans on dentists' intention to extract teeth. While these researchers did not measure actual behaviour as an outcome, they found that this simple strategy was successful in changing the behavioural intentions of professionals in line with guidelines in this area of dentistry.

1.4 The Current Study

1.4.1 Improving Clinician Completion of Clinical Records

To our knowledge, no previous studies involving an intervention to improve clinician completion of clinical records (electronic or otherwise) have been published. For example, a recent Cochrane review of interventions promoting information and communication technologies (ICT) usage did not identify any studies investigating better completion of electronic patient records (Gagnon et al., 2009). There has been some descriptive literature on obstacles to performing aspects of this behaviour, specifically completing and collecting patient-reported outcome measures (PROMs), from the perspective of individuals (Johnston & Gowers, 2005) and in relation to organisational, financial and regulatory factors (Bickman, 2008). This research has focused on factors affecting use of PROMs but does specifically address their documentation in electronic records.

Despite the limited research on electronic records, implementation research in other areas provides useful information to draw on when considering related quality improvement strategies (e.g. Grimshaw et al., 2004). Oxman and colleagues (1995) describe various categories of interventions to improve professional performance on an individual level, including educational materials, audit and feedback, reminders and multifaceted interventions (Table 2). There is a growing body of research on the effectiveness of these interventions in different contexts. For example, one study targeting GPs found that reminders were effective in improving radiological referrals, while an audit and feedback intervention did not result in behaviour change (Eccles et al., 2001). Overall, the research suggests that passive dissemination interventions alone are ineffective, while active interventions appear to be effective in some, but not all, situations and multi-faceted interventions are more likely to result in behaviour change (Grimshaw et al., 2001).

Table 2: Types of interventions described in implementation research (taken from Oxman et al., 1995).

Intervention Type	Example
1. Education Materials	Printed information materials
2. Conferences	Workshops, conferences
3. Outreach Visits	Visit by academic expert
4. Local Opinion Leaders	Champion nominated by professionals
5. Patient Mediated Interventions	Service User survey
6. Audit and Feedback	Summary of clinical performance
7. Reminders	Prompt to carry out a specific behaviour
8. Marketing	Focus groups to identify barriers to change
9. Multi-faceted Interventions	Combination of simple interventions
10. Local Consensus Processes	Consultation to ensure behaviour is important

1.4.2 Aims

The aim of the current study was to draw on the theories and previous research described above in order to develop, implement and evaluate an intervention to improve clinician completion of electronic clinical records in a

specialist child and adolescent mental health service (CAMHS). The specific objectives were to:

1) To identify clinician-reported obstacles to completion of required clinical record fields
2) To describe the baseline completion rates of the required fields via an audit of clinical record completion
3) To develop an intervention to improve completion of these fields
4) To implement this intervention within the service for a period of three months
5) To evaluate the effect of the intervention via a post-implementation audit of clinical record completion

2 Method

2.1 Service Context

2.1.1 Service Setting

The study was conducted in the Anxiety and Traumatic Stress Service for Children and Young People ("The Child Anxiety Clinic"), which functions as a "National and Specialist" outpatient service within the wider CAMHS Directorate of South London and Maudsley NHS Foundation Trust (SLaM). The team offers clinic-based assessment and treatment (individual and family-based cognitive behavioural therapy) for anxiety disorders and related problems in children and young people aged up to 18 years. The team is unidisciplinary and consists of qualified clinical psychologists (permanent staff) and trainee clinical psychologists (undertaking temporary six-month placements).

2.1.2 Standards

In common with most other SLaM services, clinical information about cases seen at the Child Anxiety Clinic is recorded on the secure Electronic Patient Journey System (ePJS). It is expected that all staff, both permanent and temporary, attend Trust training in the use of ePJS and have access to relevant data recording policies issued by SLaM and the CAMHS Directorate and Trust policy guidance. These policies include information on clinical record keeping and the quality of records (SLaM, 2010a; 2010b; 2011).

In particular, these policies identified that the (1) diagnosis (ICD-10), (2) risk (CAMHS Brief Risk Screen) and (3) care plan (Mental Health Care Plan) fields must be completed following every initial assessment in CAMHS services in the Trust. Furthermore, these policies state that routine outcome measures must be collected, and in CAMHS these were identified as the (4) parent-

reported Strengths and Difficulties Questionnaire for parents of 3-16-year-olds (SDQ-parent), (5) the child-reported SDQ for 11-17-year-olds (SDQ-child) and the (6) clinician-reported Child Global Assessment Scale (C-GAS). Timeframes for completion of these records generally state that 'best practice' involves completion of fields on the same working day as the initial assessment or within 72 hours after first contact as a 'minimum standard'. The exceptions were the ICD-10 diagnosis and Care Plan, which should be completed within 7 days, and the assessment letter (as a 'written assessment record'), which should be completed within 2 weeks (Table 3). Several other clinically relevant data fields were also identified. These additional audited fields included the Event Note, assessment fields (represented by "Presenting Circumstances") and sending a letter to the referrer in a timely manner (defined by team consensus as within two weeks of the assessment taking place).

Table 3: Audited electronic clinical record fields and expected completion times

ePJS Field	Best Practice	Minimum Standard
Multi-axial ICD 10[a,b,c]	Same working day[a]	Within 7 days[a]
CAMHS Brief Risk Screen[a,b,c]	Same working day[a]	Within 72 hours[a]
Care Plan Mental Health[b,c]	Same working day[d]	Within 7 days[d]
C GAS[a,c]	Same working day[a]	Within 72 hours[a]
SDQ (Parent)[a,c]	Same working day[a]	Within 72 hours[a]
SDQ (Child)[a,c]	Same working day[a]	Within 72 hours[a]
Presenting Circumstances[a,b,c]	Same working day[a]	Within 72 hours[a]
Event Note[c]	Same working day[d]	Within 72 hours[d]
Attachment (Letter to referrer)[a,c]	Within 1 week[d]	Within 2 weeks[b]

[a]Source: Data Quality Policy (SLaM, 2010a); [b]Source: Clinical Records Policy (SLaM, 2010b; [c]Source: CAMHS ePJS Guide (SLaM, 2011); [d]Timeframe based on team consensus

2.2 Design

This study involved two phases. The developmental phase involved formative work to develop an intervention aimed at improving completion of clinical records. This phase drew on relevant theory, empirical evidence and

stakeholder's perspectives. The evaluation phase involved an investigation of intervention effects using a pre-post cohort design. This incorporated a comparative audit of the 'baseline' completion rates and 'post-implementation' completion rates. The plan was for both the baseline and post-implementation audit windows to have a duration of three months, as it was estimated that this time would include a sufficient number of initial assessment cases.

2.3 Participants

Participants receiving the intervention consisted of clinical staff based in the Child Anxiety Clinic. Team members during the baseline and post-implementation audit windows are described in Table 4. Four of the initial seven team members were consistent throughout the study and three staff members changed between the baseline and post-implementation audit periods. An additional team member joined the service between the two audit windows.

Table 4: Team Members during the baseline and post-implementation audit windows

Position	**FTE***	**Staff Membership**	
		Baseline	Post-Implementation
Hon. Cons. Clinical Psychologist	0.2	✓	✓
Hon. Cons. Clinical Psychologist	0.2	✓	✓
Consultant Clinical Psychologist	1.0	✓	
Clinical Psychologist	0.6	✓	✓
Clinical Psychologist	0.2	✓	✓
Clinical Psychologist	1.0		✓
Clinical Psychologist	0.5		✓
Trainee Clinical Psychologist	0.6	✓	
Trainee Clinical Psychologist	0.6	✓	
Trainee Clinical Psychologist	0.6		✓
Trainee Clinical Psychologist	0.6		✓

*Full Time Equivalent, where 1.0 represents full time employment (10 sessions per week)

2.4 Development and Implementation of Intervention

A literature review was conducted to identify previous approaches to improving completion of routine clinical records and outcome measures. As no previous interventions appropriate to the current service need had been described in the literature, it was necessary to identify the factors relevant to the service and develop a set of interventions based on this formulation. Useful principles that could be included in the development of such an intervention were identified from previous literature, in particular, concepts drawn from the TPB and other social cognitive theories (Ajzen, 1991; Michie et al., 2005). These principles formed the basis of a semi-structured interview with team members on their routine record keeping views and behaviour (Appendix 1). Six of the seven team members agreed to participate in these interviews. Efforts were made to seek the views of the seventh team member, for example by creating a brief questionnaire which could be completed at a convenient time, but this was not possible. These interviews were recorded and later transcribed and summarised.

Different themes arose from the interviews depending on the position of the interviewee. Permanent members of the team reported good *knowledge* of the standards laid out in trust policies in general, but raised specific concerns about completion of some fields, for instance the appropriateness of adding a diagnosis after a single assessment session in all cases (*beliefs about consequences*). Permanent members of the team reported that time was also an issue due to competing clinical demands (*environmental context and resources*). Some team members, in particular those working part time (e.g. working one day per week in the service), noted that it was not always feasible to complete records within the recommended time frames. In contrast, trainee members of the team cited lack of knowledge as an obstacle to completing the fields, in particular due to avoidance because of reduced confidence in the quality of information recorded (*knowledge; beliefs about capabilities*). Furthermore, seeking clarification from the clinical supervisor or the team frequently delayed completion of the fields beyond the appropriate

timeframe (*skills; environmental context and resources*). Some team members from both groups felt that they occasionally forgot to complete these fields when they were not completed immediately *(memory, attention and decision making*). Other issues were raised by team members, including off-site access to the clinical record system and allowing administrators access to input non-sensitive data, but these were beyond the scope of the current study to implement.

Table 5: Proposed Interventions arising from the staff consultation interviews.

Intervention Name	Description
Team Reference Guide	Provides information on which fields to complete, how and when to complete them. Summarises Trust policies in an accessible format as applied to the team.
Checklist of fields	A list of the required fields to complete, alongside the recommended timeframes for completion, which should be ticked off on completion after each initial assessment
Clarified team Guidelines	Developing a team consensus guideline on issues which are not addressed in trust policies (e.g. what code to record if diagnosis requires further assessment)
Protected time after assessments	Protected time after an initial assessment to enter routine clinical record data following the assessment. In the case of trainees being requested to enter data, this time should be used to agree the data to be recorded.
Team monitoring	Clinical records to be permanently added to the team meeting agenda, in order to ensure all service users have a full minimum data set
Induction materials	Greater emphasis on clinical records during induction training for new team members (including trainees) with clear written guidelines

Based on the themes arising from the interviews, a number of possible interventions were identified by the study author and supervisor (Table 5). These potential intervention components were discussed in a team meeting in

order to verify their relevance and feasibility. Consistent with TPB and existing literature on health professionals' behaviour change, it was recommended that a multi-faceted intervention would be implemented. Consensus was reached that this would include: (1) feedback on current recording performance in the team; (2) educational materials detailing the required clinical data fields to complete in the service [Appendix 2]; (3) checklist of data recording actions after initial assessment to serve as a reminder [Appendix 3]; (4) regular recording of fidelity during weekly team meetings. A consensus was also reached in the team regarding the key standards, which were consistent with Trust policy.

The results of the initial baseline audit were presented to the team to highlight the current standard of record keeping and to provide a rationale for the need for intervention. At the request of the team managers, the details of services users with missing data were shared with the clinicians responsible for entering this data, so that these omissions could be corrected. Once the intervention was agreed by the team and intervention materials were finalised, these were presented to the team in a team meeting. Individual teams members were provided with paper copies of the intervention materials, as well as electronic copies, which could be given to new team members during their induction to the service. This team meeting marked the beginning of the post-implementation audit period.

2.5 Measures

The six standards and timescales listed in Section 3.1 above were identified as the primary fields to audit. The additional fields identified as clinically relevant were also included. These standards were converted into a specially designed audit proforma. This recorded the age of the service user assessed, the date of assessment, whether they stayed in the service to receive treatment and the date of entry of each of the audited electronic clinical record fields. In cases where fields were not completed at any time after the

assessment session, this was recorded. It was beyond the scope of this study to assess the quality of data recording in any other ways (e.g. accuracy) apart from presence, absence and timeliness of data entry within specific fields. Hence, the audit form was designed according to the following categories: “Completed in Best Practice Timeframe”, “Completed in Minimum timeframe”, “Completed late”, “Not completed”.

2.6 Procedure

Clinical governance approval was received from the SLaM CAMHS Audit Committee prior to commencement of data collection. The baseline audit took place between February and April 2011 and all service users who attended for initial assessment at the service during this period were included as cases. Data from the identified fields were extracted from ePJS, where possible, by the SLAM information manager six weeks after the end of the audit window. These extracted data consisted of programmed outputs obtained directly from the ePJS information server, and included the dates of completion of the relevant fields during the audit window, for each case included in the baseline cohort. This information was then checked manually to ensure that the listed dates were associated with the index assessment, and to ensure that the recorded date was the actual date of completion of the field (as recorded automatically by ePJS), rather than the date manually entered by the clinician (which can be any date, retrospectively entered). As not all the data fields could be extracted using programmed outputs (e.g. upload date of the letter to the referrer), these additional data were gathered manually. The final data set was compared to the identified standards and coded on the audit proforma (Appendix 4).

The second audit phase included data from all assessments in the four months following implementation of the intervention (between October 2011 and January 2012) and involved extracting data for all service users who underwent initial assessment during the four months following implementation

of the intervention. This audit window had been extended by an additional month in order to increase the number of service users in the post-implementation cohort, as fewer referrals for initial assessment were received during this period. These data were extracted six weeks after the end of the audit window using the same procedure as for the baseline audit (Appendix 5).

2.7 Analytic Plan

Descriptive data on the cases assessed during the audit periods will include: (1) the number of cases assessed, (2) whether the service user continued to be seen for treatment post-assessment and (3) the age range of each service user (>10 years or 11≤ years). This 'age category' is important as only young people aged 11 years or older are asked to complete the SDQ themselves. Completion rates will be presented in terms of percentage completion in line with each standard for both audit periods.

In order to assess the statistical significance of changes in routine clinical record keeping, the two sets of data (pre- and post-implementation) were compared using Pearson's Chi Squared analyses. Where the expected data count was less than 5 in any cell, Fisher's Exact Test was used to control for this.

3 Results

3.1 Case Characteristics

In total, 28 cases were assessed during the 3-month baseline audit period. Of these, 22 continued to be seen by the service for treatment, and 14 of the 28 clients were under the age of 11 years. Seventeen cases were assessed during the 4-month post-implementation audit period, of which 15 received treatment. Six of these 17 cases were under the age of 11 years.

3.2 Baseline and Post-Implementation Audit

The baseline audit assessed the completion rates of the six primary fields and the three additional fields (Figure 2). 'Anytime completion' rates for the six primary fields (up until the data were collected) ranged from 64.3% to 85.7%, with completion of the additional fields falling between 50% and 89.3%. Completion rates within the Minimum timeframe fell between 35.7% and 67.9% for the primary fields and between 14.3% and 64.3% for the additional fields. Completion rates within the Best Practice timeframe were similar to the Minimum timeframe (primary fields: 28.6% to 64.3%; additional fields: 0% to 46.4%). In summary, between 35.7% and 14.3% of the primary fields were not completed during the baseline period, and between 50% and 14.3% of the additional fields were not completed.

The post-implementation audit re-assessed completion rates of all fields (Figure 3). 'Anytime completion' rates for the six primary fields ranged from 70.6% to 90.9%, and the equivalent rates for the additional fields were 52.9% to 100%. Cumulative Minimum timeframe completion rates fell between 58.8% and 76.5% and 52.9% and 94.1% respectively. Completion rates within the Best Practice standard were between 29.4% to 54.5% for the primary six fields, and between 29.4% and 52.9% for the additional fields. Therefore, during the post-implementation period between 29.4% and 9.1% of the

required fields were not completed, and the percentages not completed for the additional fields lay between 47.1% and 0%.

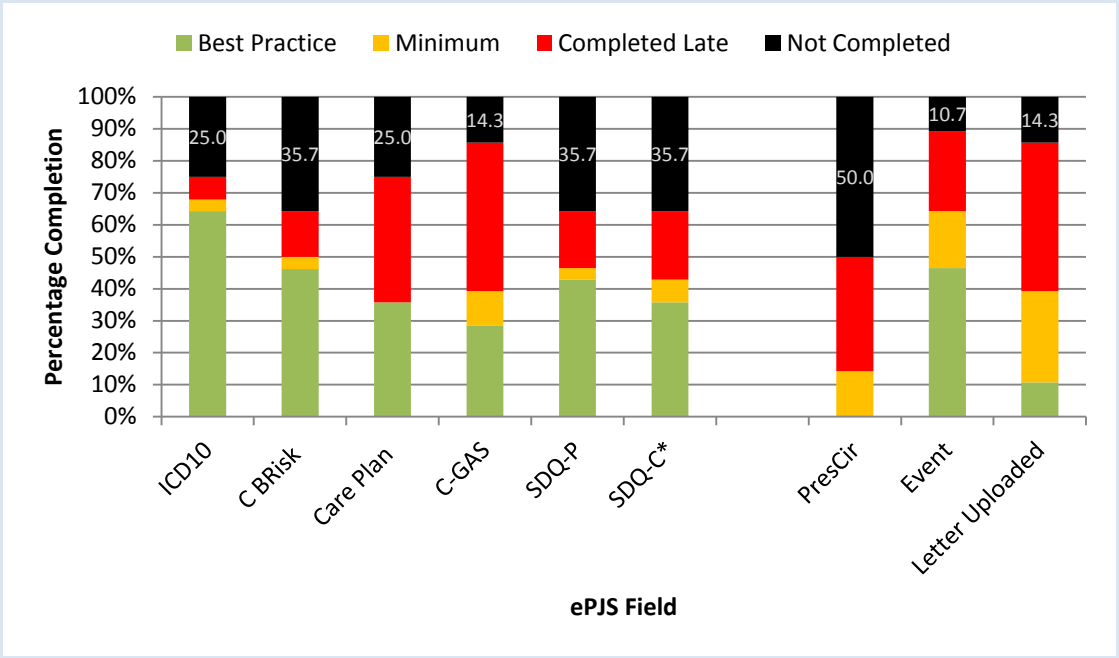

Figure 2: Percentage completion of ePJS fields by time category for the Baseline Audit period (n = 28, *SDQ-C n = 14).

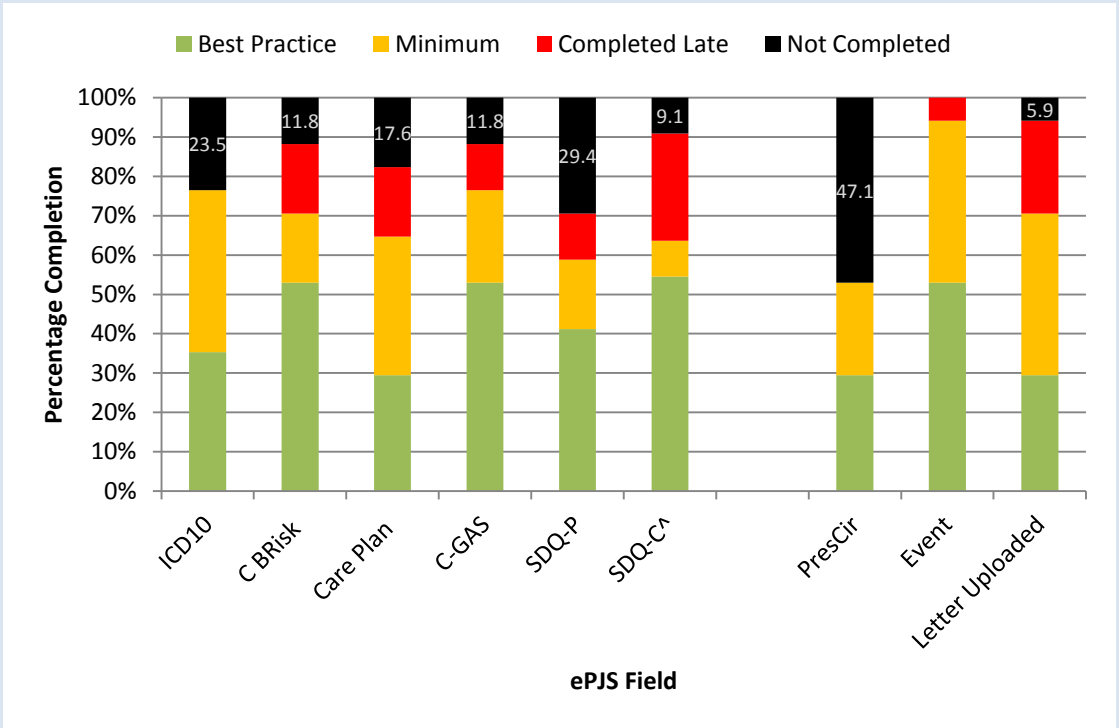

Figure 3: Percentage completion of ePJS fields by time category for the Post-Implementation Audit period (n = 17, ^SDQ-C n = 11).

3.3 Evaluation of the Effectiveness of the Intervention

The change in completion rates between the pre- and post-implementation periods are presented in Figures 4 to 6. The statistics relating to pre and post-implementation differences in completion rates are presented in Tables 6 and 7.

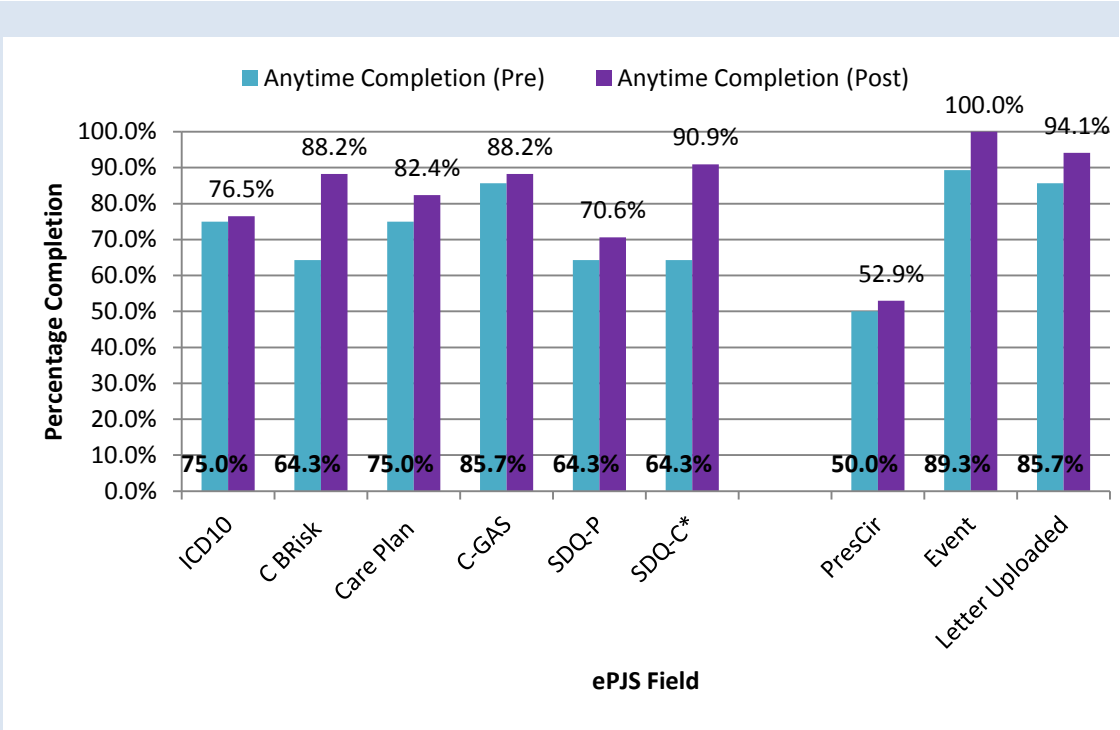

Figure 4: Comparison of Baseline and Post-Implementation completion rates of the ePJS fields at any time during the audit period

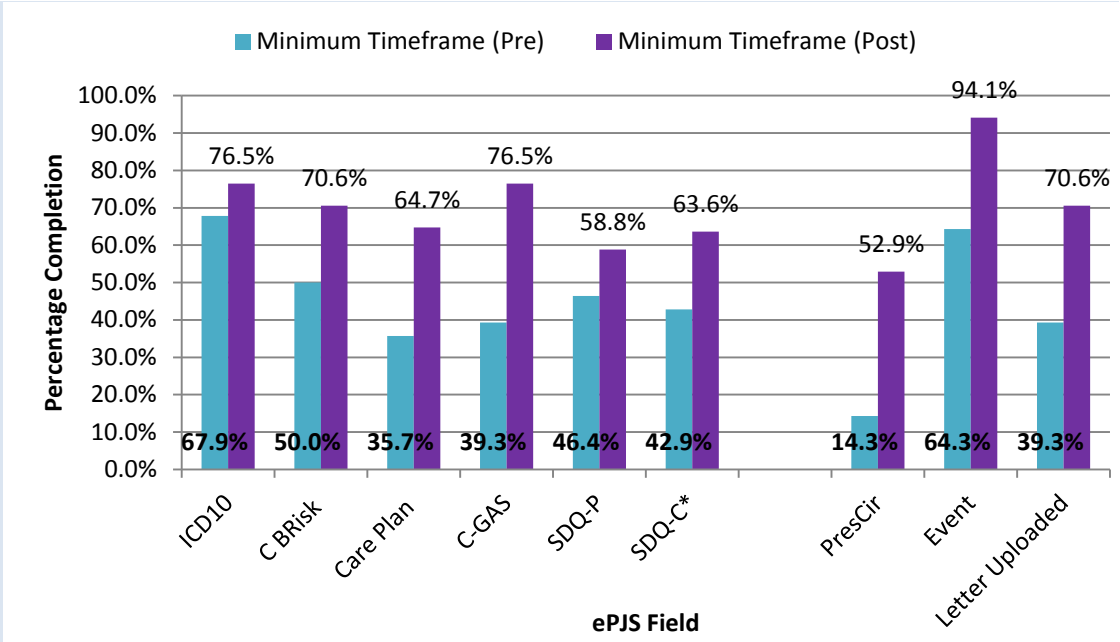

Figure 5: Comparison of Baseline and Post-Implementation completion rates of the ePJS fields in line with the Minimum Standard (either completion within 72 hours or within 7 days of initial contact)

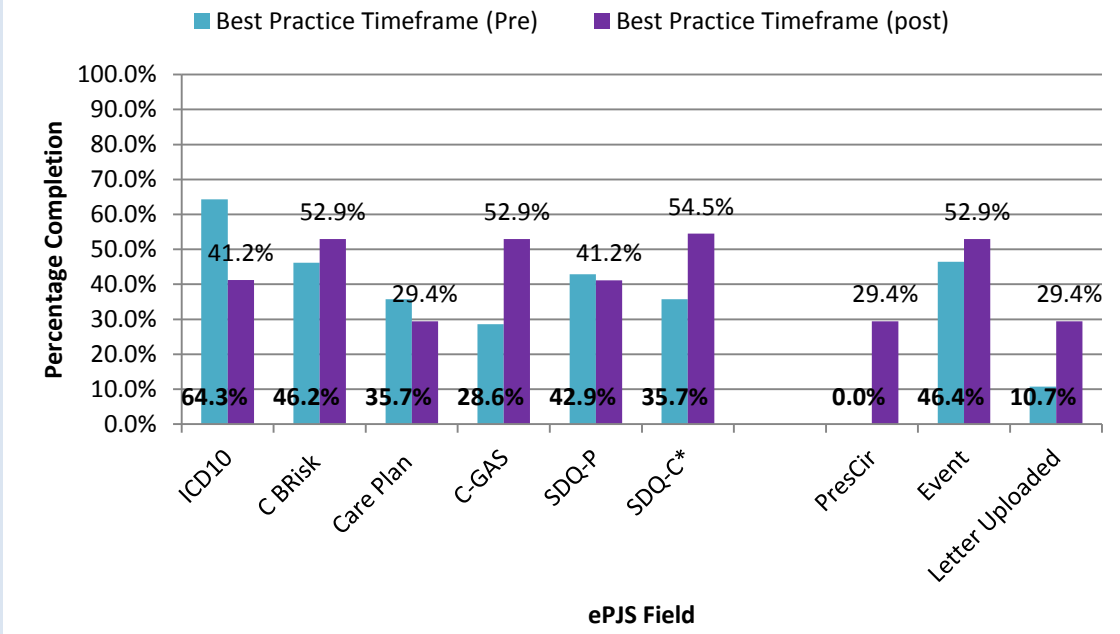

Figure 6: Comparison of Baseline and Post-Implementation completion rates of the ePJS fields in line with the Best Practice Standard (completion on the same working day as the initial assessment)

Table 6: Percentage completion rates of the primary audited fields as compared to Best Practice, Minimum and Anytime Completion standards

Standard	ePJS Field	Baseline (%) n = 28	Post Implementation (%) n = 17	Change (%)	χ^2 Statistic	p value
Best Practice	ICD-10 Diagnosis	64.3	41.2	-23.1	2.288	.115
	Child Brief Risk Screen	46.2	52.9	+6.7	0.180	.454
	Mental Health Care Plan	35.7	29.4	-6.3	0.189	.461
	C-GAS	28.6	52.9	+24.3	2.67	.094
	SDQ-Parent	42.9	41.2	-1.7	0.012	.581
	SDQ-Child (n = 14 / 11)	35.7	54.5	+18.8	0.540	.368
Minimum	ICD-10 Diagnosis	67.9	76.5	+8.6	0.382[a]	.395
	Child Brief Risk Screen	50.0	70.6	+20.6	1.838	.148
	Mental Health Care Plan	35.7	64.7	+29.0	3.572	.057
	C-GAS	39.3	76.5	+37.2	5.877	.016*
	SDQ-Parent	46.4	58.8	+12.4	0.650	.309
	SDQ-Child (n = 14 / 11)	42.9	63.6	+20.7	1.066	.265
Anytime Completion	ICD-10 Diagnosis	75.0	76.5	+1.5	0.012[a]	.602
	Child Brief Risk Screen	64.3	88.2	+23.9	3.103[a]	.076
	Mental Health Care Plan	75.0	82.4	+7.4	0.331[a]	.426
	C-GAS	85.7	88.2	+2.5	0.058[b]	.593
	SDQ-Parent	64.3	70.6	+6.3	0.189	.461
	SDQ-Child (n = 14 / 11)	64.3	90.9	+26.6	2.394[b]	.141

[a]1 cell has an expected count less than 5; [b]2 cells have expected counts less than 5; * $p < 0.05$

Table 7: Percentage completion rates of the additional audited fields as compared to Best Practice, Minimum and Anytime Completion standards

Standard	ePJS Field	Baseline (%) n = 28	Post Implementation (%) n = 17	Change (%)	χ^2 Statistic	p value
Best Practice	Presenting Circumstances	0.0	29.4	+29.4	9.265[b]	.005***
	Clinical Event note	46.4	52.9	+6.5	0.180	.454
	Letter Uploaded	10.7	29.4	+18.7	2.530[b]	.118
Minimum	Presenting Circumstances	14.3	52.9	+38.6	7.694[a]	.008**
	Clinical Event note	64.3	94.1	+29.8	5.097[a]	.024*
	Letter Uploaded	39.3	70.6	+31.3	4.148	.041*
Anytime Completion	Presenting Circumstances	50.0	52.9	+2.9	0.037	.546
	Clinical Event note	89.3	100.0	+10.7	1.952[b]	.231
	Letter Uploaded	85.7	94.1	+8.4	0.756[b]	.365

[a]1 cell has an expected count less than 5; [b]2 cells have expected counts less than 5; *p < 0.05; ** p < 0.01; *** p < 0.005

With regard to change in the completion of fields at any time, the completion rates increased across all audited fields, although these increases were not found to be statistically significant. The percentage increase for the six primary audited fields ranged from 1.5% to 26.6%. For the additional fields, the increases ranged from 2.9% to 10.7%.

In relation to the Minimum standard timeframe, again completion rates for all audited fields increased. The largest increase of the primary audited fields was for the C-GAS (37.2% increase) and this was found to be statistically significant (χ^2 = 5.877, p = .016). No other increase was found to be significant for these fields. For the additional audited fields, completion rates were found to have significantly improved for all three fields: Presenting Circumstances (χ^2 = 7.694, p = .008), Clinical Event Note (χ^2 = 5.097, p = .024), Letter Uploaded to ePJS (χ^2 = 4.148, p = .041).

Finally, the pattern was more mixed for the proportion of cases meeting the Best Practice standard timeframe. The completion rates for three audited fields increased (from 6.7% to 24.3%) while it decreased for the remaining three fields (from -1.7% to -23.1%), although none of these changes were significant. Completion rates of the additional audited fields all showed improvements (2.9% to 10.7%) but these did not reach statistical significance.

4 Discussion

4.1 Summary of Main Findings

This study has shown that it is possible to develop and implement a feasible, theoretically-derived service intervention to improve clinical record completion in routine CAMHS practice. The views of participating team members on clinical record completion were explored through individual interviews with team members using concepts from social cognitive theories, including the TPB and the related healthcare implementation framework described by Michie and colleagues (2005). The information about clinicians' behaviour beliefs and obstacles to clinical record-keeping gathered from these interviews was used to develop several possible interventions to support staff to improve record completing behaviour. The research literature on improving professional practice was drawn on to develop a multifaceted intervention to tackle this issue (Oxman et al., 1995) including the use of audit and feedback, local consensus processes, reminders and educational materials.

The intervention was associated with an increase in completion rates across a number of clinical record fields. In particular, completion rates increased for all fields compared to "Minimum Standard" timescales. Nevertheless, completion rates remained below the Trust's predetermined standard of 100% completion. At baseline, the absolute completion rates for the majority of fields fell between 60% and 75%, and completion rates typically fell between 35% and 50% for the Minimum standard timescale. The results of this audit confirm the importance of developing an intervention to increase clinician completion of these routine clinical records.

The post-implementation audit demonstrated an improvement in clinician completion of the required fields, with the largest improvements observed when completion rates were compared to the 'Minimum' timescale standard.

For this standard, there was an increase in completion rates of 20% or more for seven of the nine audited fields, of which three of the fields showed a statistically significant increase (C-GAS, Presenting Circumstances, Event note). The results indicated that there was a statistically significant increase in the proportion of assessment letters completed on time. With regard to the two audited fields which did not show large improvements (ICD-10 diagnosis, SDQ-parent report), it may be that other factors limited the amount by which completion rates could increase. The ICD-10 field showed the highest completion rate at baseline, limiting the potential for improvement. The SDQ-parent questionnaire requires the direct co-operation of the families of service users, and this was not targeted by the current intervention, limiting the potential for change. Interestingly, a small number of completion rates decreased compared to the 'Best Practice' standard following implementation. It is hypothesised that the intervention created a shift in the clinicians' intentions and behaviour so that they aimed to consistently complete fields within the minimum acceptable timeframe. This is supported by the fact that there was a corresponding increase in Minimum standard completion rates for these three fields.

Relating the findings of the study to the TPB and related theories, it can be seen that targeting the cognitions of staff members, through individual interventions, can lead to an improvement in target behaviours, in this instance an increase in clinical record completion in line with standards. In particular, team members identified obstacles to performing the behaviour (i.e. factors related to perceived behaviour control) such as lack of knowledge and perceived lack of time, as well as low expected value (i.e. attitude) such as low priority of the behaviour compared to other clinical tasks. Interventions chosen to target these problems and associated cognitions led to improvements in the target behaviour. However, this study did not directly measure cognitions and therefore cannot comment on whether changes in the cognitions of team members mediated the change in observed behaviour.

While the intervention was successful at changing behaviour, post-implementation completion rates remained below the expected 100% completion. This sub-optimal implementation of guidelines has been reported elsewhere in the literature on changing clinicians' behaviour (e.g. Laws et al., 2009). In considering this sub-optimal implementation, it is useful to draw on theory and previous research. Firstly, in terms of theory, it is important to note that this study focused on obstacles to completing the behaviour, rather than on directly shifting subjective norms or attitudes towards the behaviour. Given that passive educational programmes have generally been found to be ineffective at changing behaviour, it may be that a more active process could be beneficial. One such approach described in the literature involves brief education sessions drawing on cognitive behaviour therapy (CBT) principles to challenge the attitudes of professionals. For example, Treloar (2009) investigated the effects that a two hour education programme had on the beliefs and attitudes of professionals working with people with borderline personality disorder.

Secondly, previous research has suggested that these variables account for a moderate amount of the variance in actual behaviour, and this is in keeping with the current study, which demonstrated moderate increases in completion of clinical records. This suggests that research relying solely on TPB concepts may fail to account for all relevant factors and thus may fail to achieve 100% completion rates. Other relevant factors may include broader systemic, rather than individual, factors with some suggestion that interventions need to account for the complex interactions between the intervention and the service context (e.g. Greenhalgh et al., 2004; Grol et al., 2007). For instance, it may be that clinicians need extra time to follow guidelines on clinical records (organisational context) but that no financial compensation is available for working extra time (economic context). In this example, effective interventions may need to address organisational factors to overcome obstacles to carrying out the target behaviour.

4.2 Recommendations and Implications for the Service

This study has shown that a systematic intervention focusing on changing clinician behaviour can make a significant difference to routine data recording. Therefore, the first recommendation arising from this study is the routinisation of the interventions in the service to maintain the improvements observed. However, additional activities may be required to influence clinician behaviour to the extent that completion rates approach 100%. One observation while conducting this study was that some service users had data recorded by another service shortly before the initial assessment in the Child Anxiety Team, in particular, those service users who had been referred on to the team immediately following assessment due to the complexity or nature of their presentation. In these cases, clinicians were less likely to complete the fields again, and this contributed to the sub-optimal completion rates. Thus, a second recommendation therefore would involve clarifying the policy about whether fields need to be duplicated when they have been recently completed by another service.

Other methods to increase completion of clinical records should be explored and evaluated. For example, it may be that the educational materials provided should be more specific and tailored to the precise issues raised by staff, in this case what information to record in atypical circumstances not covered by generic guidelines (e.g. what diagnosis to record if no diagnosis has been arrived at following the initial contact). As noted above, it may also be useful to provide tailored educational sessions to elicit and challenge clinicians' attitudes and assumptions about following guidelines on clinical record keeping.

It would also be useful to repeat the audit in the future in order to assess the sustainability of changes in practice. The intervention materials should be revised and improved based on feedback from team members and information on other obstacles. As accurate and timely clinical records become increasingly necessary in the future, failure to improve practice in this

regard may lead to action being taken by the Trust, commissioning bodies or government organisations.

4.3 Dissemination of Results

The results of the baseline audit were presented in the Child Anxiety Clinic team meeting prior to development of the intervention. Results of the full project were fed back to the Child Anxiety Clinic once the post-implementation audit was completed and analysed. This feedback involved presenting a summary of the completed study during a team meeting, with a question and answers session to discuss the study and the recommendations.

Following feedback, the service has continued to use the intervention materials. This can be seen as an endorsement of the consultative methods used to involve team members in the developmental stages. The resulting checklist of procedures and guidance notes can be used routinely with a minimum of additional training. These are provided to all new trainee members of the team, who typically take the lead in completing electronic records for new assessments.

The study was also summarised in a Management Summary Report which was disseminated to the Child Anxiety Clinic, the CAMHS Information Manager, service managers for CAMHS and the director of clinical governance. This report included recommendations for routinisation of the interventions, and prospective audits.

4.4 Methodological Issues

A number of methodological considerations are relevant in interpreting the results of this study. As a general point, it is important to note that the study addressed individual behaviour through interventions aimed at professionals, rather than making changes at higher levels, such as organisational or economic contexts, as detailed above. Firstly, the service consists of a small

team, and therefore the number of clinicians receiving the intervention were few. This may have led to a disproportionate effect of the behaviour of a minority of clinicians. Similarly, there was a change in team members between the baseline and post-implementation audit periods, with different clinicians in both trainee clinical psychologist roles and a change in one of the clinical psychologist roles. Nonetheless, all members of the team during the post-implementation audit period received the intervention.

The number of cases assessed during the audit windows was small, which may have limited the power of the statistical analyses used to detect significant differences between the two audit phases. This can increase the probability of Type II errors. Type I error rate may also have been raised, as multiple comparisons were carried out, thus increasing the likelihood that a significant difference will be incorrectly found.

There was a difference in the number of service users seen for initial assessment by the service during the baseline and post-implementation audit windows. This may have confounded results because of reduced demands on clinicians' time during the post-intervention audit, making it easier to complete clinical record fields in line with expected standards. The number of cases during the audit periods was dependent on referrals being made to the service, and these naturally varied depending on several factors such as time of year and funding issues. In an attempt to equalise the number of cases, the post implementation period was extended to four months (compared to three months at baseline). Despite this adaptation, there were 11 fewer cases assessed during the post-implementation period.

A further methodological weakness of the study was that there was no contemporaneous control group of clinicians who did not receive the intervention materials. Again, this was due to the small number of clinicians in the service, making it unfeasible to have two groups of participants who differed only in terms whether they received the intervention. Finally,

interpretation of the study data would have been improved if the process of change had been measured. For example, it is unclear from the current findings whether all clinicians made use of the intervention materials or whether the limited improvements may be best explained by mixed uptake of the intervention amongst clinicians in the team. Although no formal measures of fidelity to the intervention were collected, the inclusion of a weekly discussion about record keeping is likely to have facilitated this during the post-implementation audit period. It would also have been useful to measure the relevant cognitions and behaviour intentions of team members before and after the intervention was implemented, to investigate whether there a simultaneous shift in record-keeping behaviour and cognitions. This could be carried out using a specially developed questionnaire based on principles from the TPB. There are several resources available for the development of such questionnaires (e.g. Francis et al., 2004).

4.5 Conclusions and Future Research

This study described a newly developed service intervention aimed at improving routine data recording which, during team consultations, was reported to be acceptable to staff. Implementation of the intervention, which comprised feedback, written guidance, checklists and weekly discussion of record-keeping, was associated with an increase in rates of data recording across all targeted fields. However, further scope for improvement was identified, with missing data noted for each of the fields. Recommendations included dissemination of the findings to the service and other CAMHS in the trust, as well on continued use of the intervention materials. Interventions to further extend improvements in recording behaviours should be explored and evaluated. The methodological limitations of this project included small and unequal sample sizes in the baseline and post-intervention audit phases, and the lack of a contemporaneous control group of clinicians who did not receive the intervention. It would be beneficial to repeat this audit in the future, while accounting for limitations arising from the methodology. Specifically, this study

should be replicated in a larger service or a group of services, to allow for a larger number of clinicians and a control group, as well as auditing a greater number of assessment cases. It would also be helpful to include measures of adherence to the intervention in any future research, as well as assessing proposed mediators of change, such cognitions and behaviour intentions.

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Appendices

Appendix 1: Format of the semi-structured clinician interview

Completion of Routine Clinical Data – Clinician Consultation			
Location:		**Date:**	
ID:		**Time:**	
Role:		**Interviewer:**	

Introduction
SLaM policies have identified a number of clinical data fields in ePJS which must be completed in a timely manner for each client on entry into the trust. These fields have been identified in policies such as the Clinical Records Policy. We are carrying out a small research project to increase the Child Anxiety Clinic's compliance with these policies.

In order to address this issue, it would be very useful to have your perspective on these policies and completion of the required fields.

I will be asking you questions about completing required data fields in ePJS in the appropriate time frame following initial assessment of newly referred children and young people.

Knowledge
How familiar do you feel with the current clinical records policies for CAMHS?
- Can you summarise what you need to complete?

Describe/show the below table:

	Field Name	Time – Best Practice	Time – Minimum
1	Child Brief Risk Screen	Same working day as assessment	72 hours after initial assessment
2	ICD-10 Diagnosis	-	Within 7 days following Initial Assessment
3	Mental Health Care Plan	Same working day as assessment	Within 7 days following Initial Assessment
4	C-GAS	Same working day as assessment	72 hours after initial assessment
5	SDQ-Parent	Same working day as assessment	72 hours after initial assessment
6	SDQ-Child version (if applicable)	Same working day as assessment	72 hours after initial assessment

General
As things stand, what systems are in place that **help** you record these data on time?

What if anything **limits** you from doing this consistently?

Skills
Thinking about the technicalities of recording this information, how do you feel about your ability to carry this out?

Beliefs about capabilities
How difficult or easy is it for you to complete these required fields within the appropriate time frame following initial assessments?

Beliefs about consequences
Thinking about the consequences of completing these fields, do you feel there are any positive or negative consequences to whether you record this data?

Motivation and goals (intentions)
Some people have said motivation to complete this task is an issue. Is this an issue for you?

Are there other things you want to achieve which might interfere with completing these fields?

Memory/Attention/Decision Processes
Do you usually complete these fields after initial assessments?

Is memory an issue when completing the fields?

Do you sometimes decide not to complete these fields following initial assessments? If so, why?

Environmental constraints and resources
Do you feel you have the resources you need to complete the fields?
- physical (computers, ePJS access)
- time

Social influences (Norms)
Is there anything the team does which helps or hinders completion of these fields?

Summary
In summary, it seems that the main issues for you are: (list)

Are there any obstacles that I have missed out on? (list)

Which of these obstacles would you say the most important?

Thinking about what might help with these issues, do you have any suggestions?

Appendix 2: Quick Reference Guide on completion of routine clinical records after initial assessments

Completion of ePJS records following Initial Assessment (Audited Fields)

Team Guidance

Child Anxiety and Trauma Clinic

September 2011

Author:

Kevin Tierney, Trainee Clinical Psychologist

Contact:

Prof Derek Bolton, Team Leader

Date of Final Report: 14th September 2011

Sources of Information: Trust Policies on Clinical Records and Data Quality, ePJS Help Pages, Team Consultation

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General Notes:	
Purpose	This document was created to provide clear information on the audited clinical data which must be recorded electronically following initial assessments.
Contact	If this document does not provide the information you require, please contact your clinical supervisor
"Assessment"	Refers to the initial face to face contact following a new referral to the team.

Risk

Field: CAMHS Brief Risk Screen

Timing: Within 72 hours of assessment

Note: Ensure you complete the "CAMHS Brief Risk Screen" rather than the "Brief Risk Screen"

This field must be completed by the responsible staff member or trainee clinical psychologist only after explicit clarification of what to say from the primary assessor.

Plan/Rev

Field: Mental Health Care Plan

Timing: Within 7 days of Assessment

What to record if treatment is delayed: In some cases, an extended assessment may be needed or treatment may be delayed until the case is allocated. In these cases, the first two sections of the Mental Health Care Plan can be completed, stating the action (e.g. "To be allocated") in the Summary of Actions/Interventions field. When the care plan is finalised, all sections should be updated as appropriate.

Outcomes

Field: C-GAS **Timing:** Within 72 hours of assessment

Note: When an assessment is carried out jointly, the C-GAS score should be discussed and jointly agreed between staff.

When to complete the C-GAS: Paired C-GAS scores are required for all young people seen within the service, including those seen only for an assessment.

The **first C-GAS** should be completed within 72 hours after the assessment ("Initial Assessment") for all young people.

A **second C-GAS** is required for all young people (even if seen for assessment only) at one or more of the following times:

- No intervention needed ("Discharge from Trust"): When discharge letter sent out. This should be done *even if the young person was seen for assessment only*.
- Referral to another team within SLaM ("Other Transfer within Trust"): When discharged from this team. This should be done *even if the young person was seen for assessment only*.
- Intervention within the team with a duration of under 6 months ("Discharge from Trust" OR "Other Transfer within Trust"): On discharge from team
- Ongoing intervention within the team over 6 months ("Other Review"): Every 6 months and again at eventual discharge

Summary descriptions for C-GAS ranges
See Appendix A for full descriptions

Field: SDQ-P **Timing:** Within 72 hours of assessment

Note: While the team administrator posts the relevant SDQ forms to the family alongside the initial appointment letter it is the clinician's responsibility to record the responses on ePJS.

Field: SDQ-C **Timing:** Within 72 hours of assessment

Note: While the team administrator posts the relevant SDQ forms to the family alongside the initial appointment letter it is the clinician's responsibility to record the responses on ePJS.

Which young people should complete the SDQ-C: All young people aged 11 to 17 years who attend for initial assessment should complete the self report version of this questionnaire.

Assmts

Field: ICD-10 **Timing:** Within 7 days of Assessment

Please select ICD-10 Multi-Axial from the drop down box.

Appendices

Appendix A: Glossary for the CGAS rating

100-91 *Superior functioning* in all areas (at home, at school and with peers); involved in a wide range of activities and has many interests (e.g., has hobbies or participates in extracurricular activities or belongs to an organised group such as Scouts, etc); likeable, confident; 'everyday' worries never get out of hand; doing well in school; no symptoms.

90-81 *Good functioning in all areas*; secure in family, school, and with peers; there may be transient difficulties and 'everyday' worries that occasionally get out of hand (e.g., mild anxiety associated with an important exam, occasional 'blowups' with siblings, parents or peers).

80-71 *No more than slight impairments in functioning* at home, at school, or with peers; some disturbance of behaviour or emotional distress may be present in response to life stresses (e.g., parental separations, deaths, birth of a sib), but these are brief and interference with functioning is transient; such children are only minimally disturbing to others and are not considered deviant by those who know them.

70-61 *Some difficulty in a single area but generally functioning pretty well* (e.g., sporadic or isolated antisocial acts, such as occasionally playing hooky or petty theft; consistent minor difficulties with school work; mood changes of brief duration; fears and anxieties which do not lead to gross avoidance behaviour; self-doubts); has some meaningful interpersonal relationships; most people who do not know the child well would not consider him/her deviant but those who do know him/her well might express concern.

60-51 *Variable functioning with sporadic difficulties or symptoms in several but not all social areas;* disturbance would be apparent to those who encounter the child in a dysfunctional setting or time but not to those who see the child in other settings.

50-41 *Moderate degree of interference in functioning in most social areas or severe impairment of functioning in one area,* such as might result from, for example, suicidal preoccupations and ruminations, school refusal and other forms of anxiety, obsessive rituals, major conversion symptoms, frequent anxiety attacks, poor to inappropriate social skills, frequent episodes of aggressive or other antisocial behaviour with some preservation of meaningful social relationships.

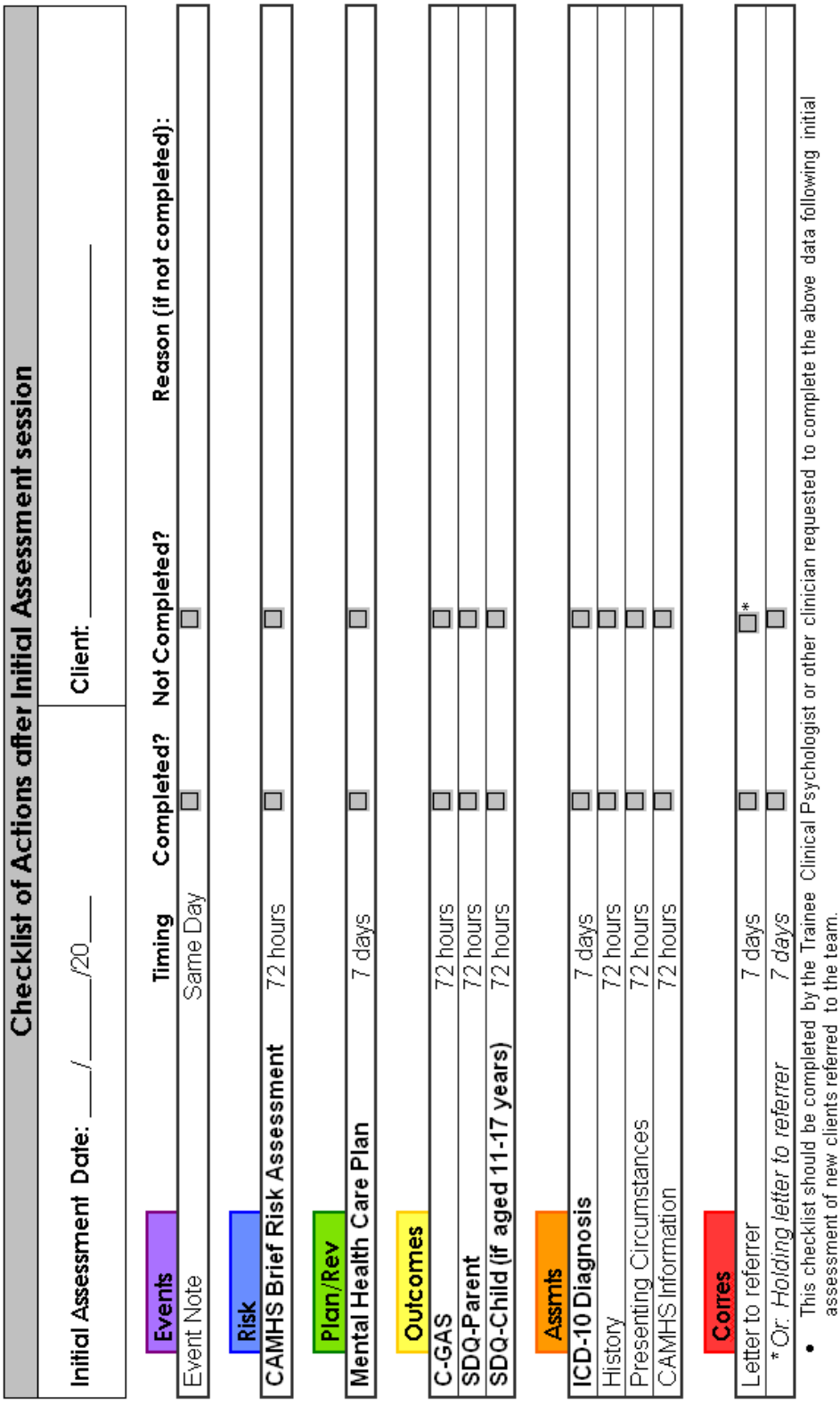
40-31 *Major impairment of functioning in several areas and unable to function in one of these areas* (i.e., disturbed at home, at school, with peers, or in society at large, e.g., persistent aggression without clear instigation; markedly withdrawn and isolated behaviour due to either mood or thought disturbance, suicidal attempts with clear lethal intent; such children are likely to require special schooling and/or hospitalisation or withdrawal from school (but this is not a sufficient criterion for inclusion in this category).

30- 21 *Unable to function in almost all areas* e.g., stays at home, in ward, or in bed all day without taking part in social activities *or* severe impairment in reality testing *or* serious impairment in communication (e.g., sometimes incoherent or inappropriate).

20- 11 *Needs considerable supervision* to prevent hurting others or self (e.g., frequently violent, repeated suicide attempts) *or* to maintain personal hygiene *or* gross impairment in all forms of communication, e.g., severe abnormalities in verbal and gestural communication, marked social aloofness, stupor, etc.

10-1 *Needs constant supervision* (24-hour care) due to severely aggressive or self destructive behaviour or gross impairment in reality testing, communication, cognition, affect or personal hygiene.

Appendix 3: Checklist of Actions after Initial Assessment Session



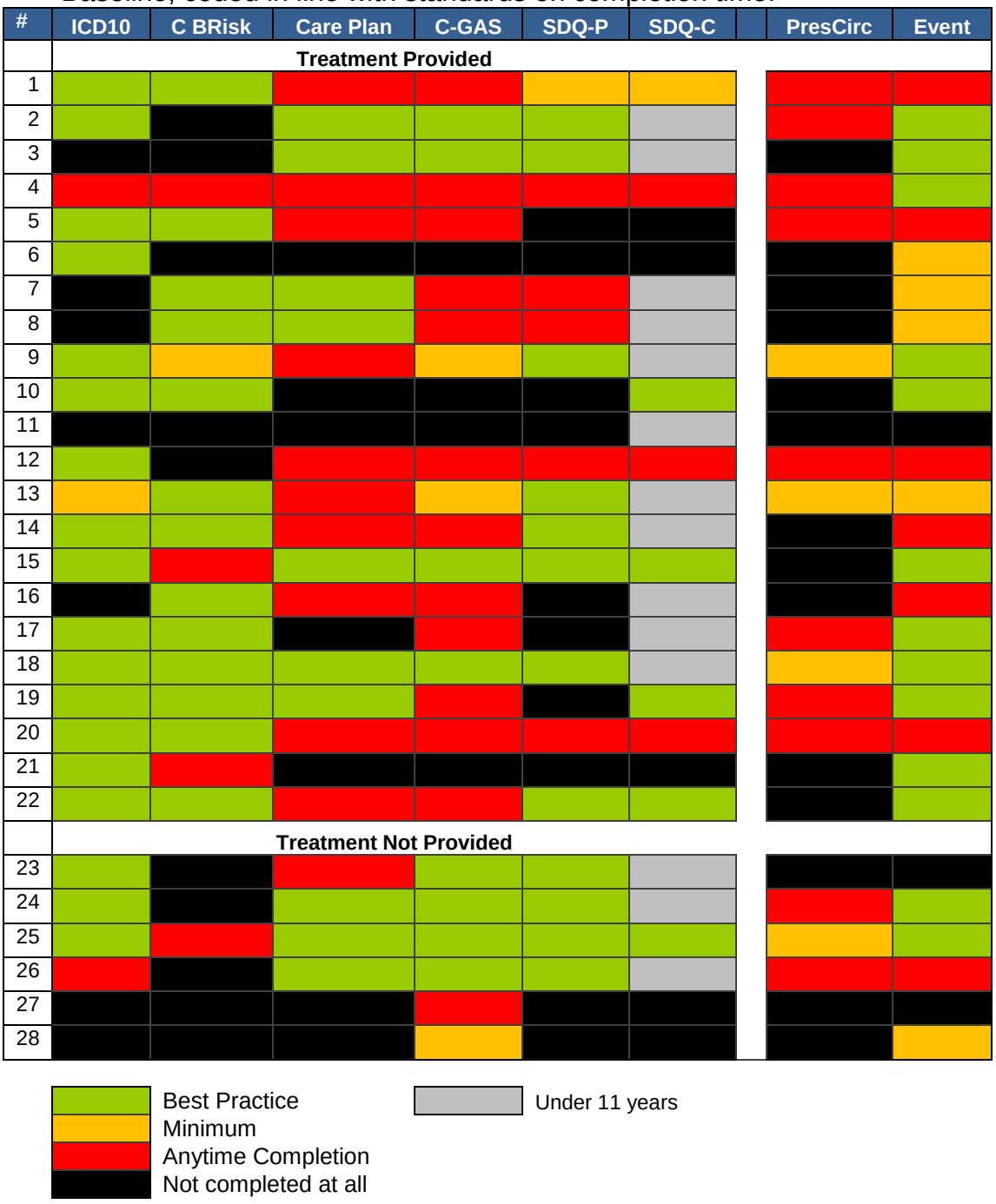
Checklist of Actions after Initial Assessment session

Initial Assessment Date: ___/_____/20___ Client: _____

		Timing	Completed?	Not Completed?	Reason (if not completed):
Events	Event Note	Same Day	☐	☐	
Risk	CAMHS Brief Risk Assessment	72 hours	☐	☐	
Plan/Rev	Mental Health Care Plan	7 days	☐	☐	
Outcomes	C-GAS	72 hours	☐	☐	
	SDQ-Parent	72 hours	☐	☐	
	SDQ-Child (if aged 11-17 years)	72 hours	☐	☐	
Assmts	ICD-10 Diagnosis	7 days	☐	☐	
	History	72 hours	☐	☐	
	Presenting Circumstances	72 hours	☐	☐	
	CAMHS Information	72 hours	☐	☐	
Corres	Letter to referrer	7 days	☐	☐*	
	*Or: *Holding letter to referrer*	*7 days*	☐	☐	

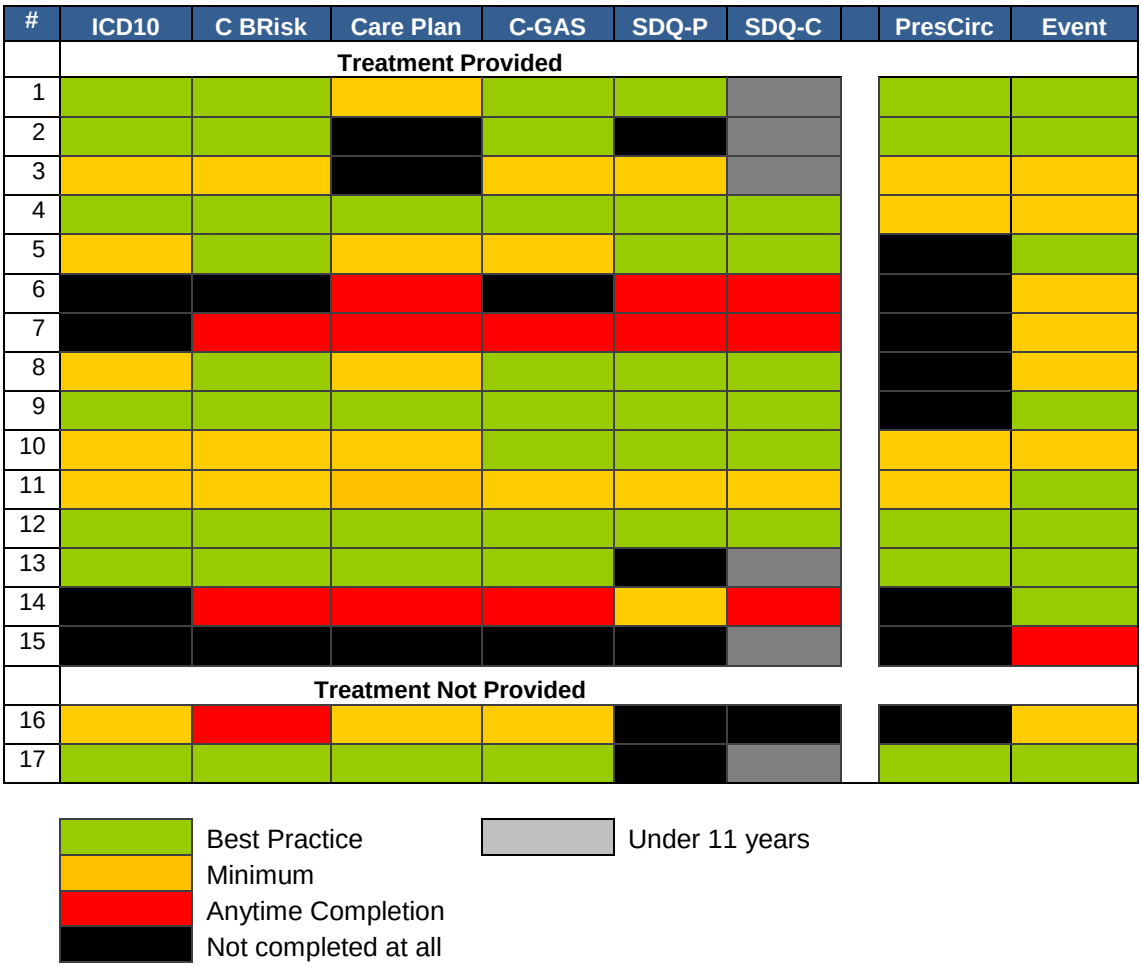
- This checklist should be completed by the Trainee Clinical Psychologist or other clinician requested to complete the above data following initial assessment of new clients referred to the team.

Appendix 4: Case by case completion rates of routine clinical fields at Baseline, coded in line with standards on completion time.



Legend: ICD10 = International Classification of Diseases 10th Edition diagnosis, C Brisk = Child Brief Risk Screen, Care Plan = Mental Health Care Plan, C-CAS = C-GAS score, SDQ-P = Parent report version of the SDQ, SDQ-C = Child report version of the SDQ (11 years + only), PresCirc = Presenting Circumstances assessment field, Event = Clinical event note.

Appendix 5: Case by case completion rates of routine clinical fields Post Implementation, coded in line with standards on completion time.



Legend: ICD10 = International Classification of Diseases 10th Edition diagnosis, C Brisk = Child Brief Risk Screen, Care Plan = Mental Health Care Plan, C-CAS = C-GAS score, SDQ-P = Parent report version of the SDQ, SDQ-C = Child report version of the SDQ (11 years + only), PresCirc = Presenting Circumstances assessment field, Event = Clinical event note.